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Design and Synthesis of Small-molecule Inhibitors of the Hypoxia Inducible Factor-1 as Anticancer Therapeutics

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DESIGN AND SYNTHESIS OF SMALL-MOLECULE INHIBITORS OF THE HYPOXIA INDUCIBLE FACTOR-1 AS ANTICANCER THERAPEUTICS

by

ZEUS ALLEN ORENCIA DE LOS SANTOS

Under the Direction of Professor Binghe Wang

ABSTRACT

Throughout history, cancer has been severely plaguing mankind; the search for a cure to cancer had long been sought by scientists and still poses as one of the greatest challenges scientists have yet to overcome. Hypoxia in cells is a condition where there is little to no oxygen availability in its environment. In general, this event is detrimental since this can lead to cell necrosis or reoxygenation injuries. However, hypoxia, a prominent property of most solid tumors, activates the hypoxia-inducible factor (HIF-1) family of transcription factors that promotes angiogenesis. In this study, we describe the design and synthesis of small-molecule inhibitors of the HIF-1 pathway.

INDEX WORDS: Hypoxia, HIF-1, Cancer, Small-molecule inhibitors

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DEDICATION

To my family, especially my mum, Vicky, who never doubted me from the very beginning and has supported me through the myriad of academic decisions I have made, may it be good or otherwise, I dedicate this work to you.

Ad Maiorem Dei Gloriam

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LIST OF ABBREVIATIONS

HIF-1	Hypoxia Inducible Factor 1
ARNT	Aryl hydrocarbon receptor nuclear translocator
PHD	Prolyl hydroxylase dioxygenase
FIH-1	Factor inhibiting HIF-1
ODD	Oxyegen degradation domain
HRE	Hypoxia response element
pVHL	Von Hippel Lindau tumor suppressor protein
VEGF	Vascular endothelial growth
NOS	Nitric oxide synthase
GLUT1	Glucose transporter 1
LDHA	Lactose dehydrogenase A
ROS	Reactive oxygen species
CBP	CREB-binding protein
AP	Alkaline phosphatase
Luc	Luciferase
SAR	Structure activity relationship
r.t.	Room temperature
DBU	1,8-diazabicyclo[5.4]undec-7-ene
$NaCNBH_4$	Sodium cyanoborohydride
PCC	Pyridinium chlorochromate
$InCl_3$	Indium (III) chloride
K_2CO_3	Potassium carbonate
KI	Potassium iodide
CuI	Copper (I) iodide

ACN	Acetonitrile
MeOH	Methanol
DCM	Dichloromethane
THF	Tetrahydrofuran

1. INTRODUCTION

1.1 Cancer and Hypoxia

Among the persistent deadly diseases mankind still face, cancer is well known as one of the most varied and tenacious. Years of research have been spent towards the search for an effective therapy that minimizes the side effects current treatments come with. Although a lot has been achieved in this field, cancer is still the second leading cause of death in the U.S.A., second only to heart attack with 186 deaths occurring per 100,000 populations.[1] Despite the tremendous amount of funding poured into research in this field, the sheer number of treatment pathways to explore is a daunting task.

Hypoxia, a pathological condition in which cells are deprived of an adequate oxygen supply, is generally detrimental to cells and tissues since the condition will eventually lead to necrosis. However, cancer cells thrive under such conditions.[2] Hypoxia is commonly seen in progressing cancer cells; the inadequate oxygen supply in cells causes tissue hypoxia, which leads to the activation of several pathways, and further development and metastasis of the tumor.[2] Cancer cells under such conditions turn on gene expressions that can alter metabolism and promote angiogenesis through multiple pathways, thereby allowing cells to fuel their progression. One example is the hypoxia-inducible factor 1 pathway (HIF-1). In tumor cells, the vasculature is different from normal cells. In addition to the normal vessels that the cells already have even before the tumor invades, most tumor cells develop microvessels that are brought about by neovascularization caused by the increased expression of genes that promote angiogenesis.[3]

1.2 Hypoxia-Inducible Factor 1 Pathway (HIF-1)

There are three members of the hypoxia-inducible factor family whose activities rely upon the concentration of oxygen in the cell (Table 1).

Table 1 Members of the Hypoxia Inducible Transcription Factor Family[4]

HIF	Function
HIF-1α	Alpha subunit, initiator of HIF function sequence
HIF-1β	Aryl hydrocarbon receptor nuclear translocator
HIF-2α	PAS domain protein
HIF-2β	Aryl hydrocarbon receptor nuclear translocator 2
HIF-3α	Alpha subunit (without transactivation domain)
HIF-3β	Aryl hydrocarbon receptor nuclear translocator 2

Although each subunit shares in the response to oxygen levels in the cell, the HIF-1 unit is the pathway that was focused on this study. The HIF-1 complex is a basic loop-helix-loop motif heterodimer that is composed of two major subunits called the HIF-1α and the HIF-1β. Levels of HIF-1α in the cells are regulated by the presence or absence of oxygen while HIF-1β is constitutively expressed as aryl hydrocarbon receptor nuclear translocator (ARNT).[5] Under normal oxygen conditions, HIF-1α gets hydroxylated by prolyl hydroxylase dioxygenase (PHD) at proline 564 and 402 and by factor inhibiting HIF-1 (FIH-1) at asparagine 803 at its oxygen degradation domain (ODD) with an iron (Fe^{2+}) and 2-oxoglutarate as co-substrates.[6] Furthermore, HIF-1α gets acetylated by ADP-ribosylation factor domain protein 1 (ARD1) at lysine 532.[7,8] This hydroxylation allows the HIF-1α to recruit the von Hippel-Lindau tumor suppressor protein (pVHL) that acts as an E3-ubiquitin ligase complex and tags the whole complex for ubiquitination and subsequent proteasomal degradation. This scenario is shown in Figure 1 as follows.

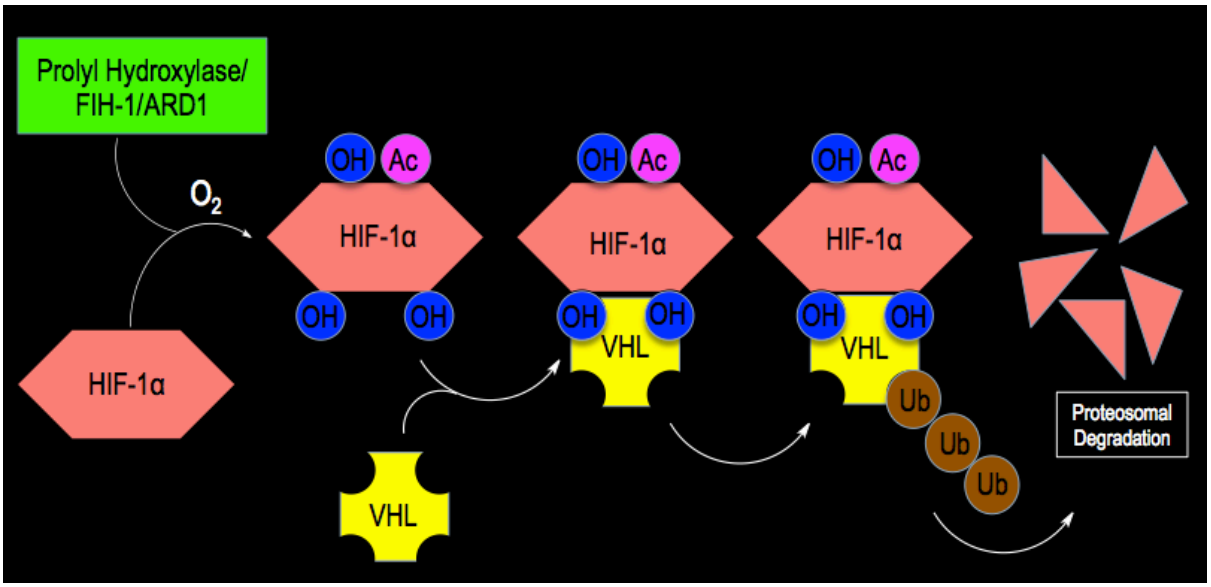


Figure 1 Proteosomal degradation pathway of HIF-1α in the presence of oxygen

As depicted in Figure 2, prolyl hydroxylase loses its function to hydroxylate HIF-1α under hypoxic conditions. The HIF-1α subunit then gets translocated into the nucleus where it binds to another HIF subunit, HIF-1β.

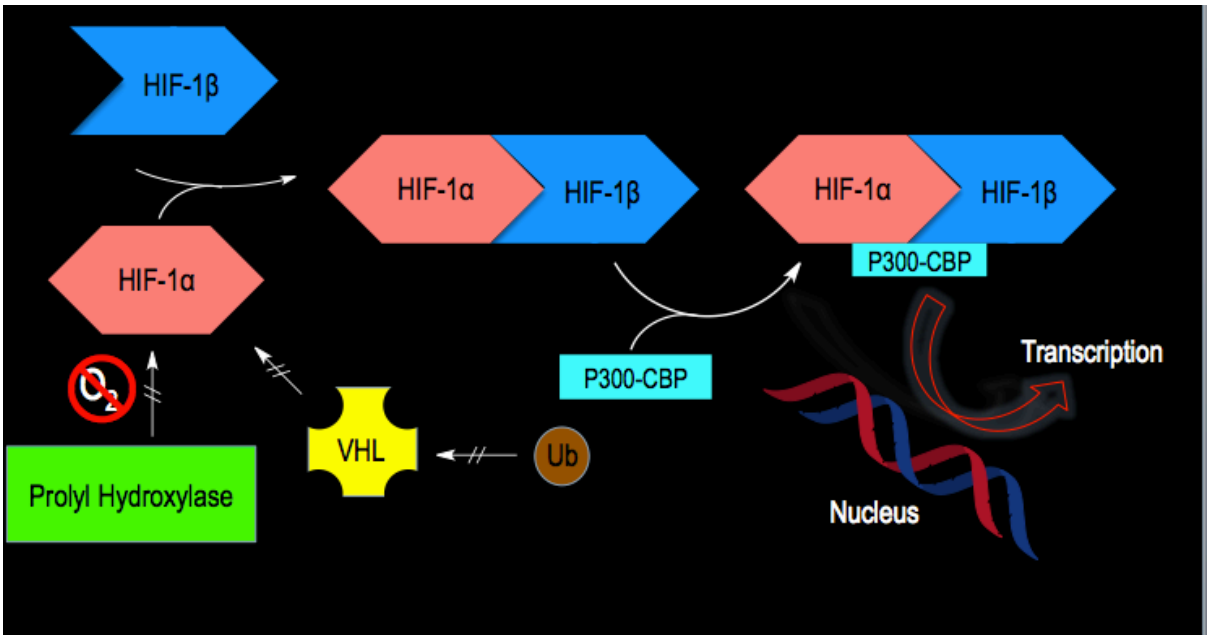


Figure 2 The HIF-1 pathway in low oxygen conditions in cells

Upon binding of HIF-1α with HIF-1β to form the active transcription factor of HIF-1, the complex then interact with its co-activator p300/CBP and binds to hypoxic

response elements (HREs) to act as a transcription factor for numerous genes.[9] Because of the importance of oxygen in cells, it is not surprising that the HIF-1 complex is a transcription factor that controls more than 2% of all human genes in arterial endothelial cells, directly or indirectly.[8] Currently, it is well understood that the HIF-1 complex affects over 100 genes, most of which are vital to a cell's survival. Among these genes are the vascular endothelial growth factor (VEGF), nitric oxide synthase (NOS), glucose transporter 1 (GLUT1), and lactose dehydrogenase A (LDHA).[10] All of these genes that were mentioned play a massive role in the proliferation of a tumor cell since they fuel its growth through the formation of new vasculature and the creation of delivery pathways to sustain its propagation.

Table 2 List of some of the genes that are activated by the HIF-1 complex[10]

Genes Activated by HIF-1	Effects on Cancer Progression
ANGPT2, C-MET, ID2, **NOS**, PGF, PDGF, SCF, SDF-1, **VEGF**	**Angiogenesis**
DEC1, MDR1	**Genetic Instability**
GLUT1, GP1, HK1, HK2, **LDHA**, PDK1, PKM2	**Glucose Metabolism**
TERT	**Immortalization**
NTSE	**Immune Evasion**
C-MET, EDN-1, FN-1, MMP-2, MMP-14, PLAU, SDF1	**Invasion**
ANGPT4, C-MET, CXCR4, LOX, MDR1, TWIST1, ZEB1	**Metastasis**
CA-IX, CA-XII	**pH Regulation**
C-MYC, ID2, IGF-2, **NOS**, PDGFB	**Proliferation**
ABCG2, JARID1B, OCT4	**Stem Cell Maintenance**

Many of the genes that the HIF-complex activates contribute to the defense mechanism of a cancer cell, as seen in Table 2. One of the most prominent features of the HIF-1 complex is that it activates genes that promote angiogenesis and glucose metabolism. Oftentimes, the cell's environment gets further aggravated because of temporary occlusions and blocked vasculatures, a condition which

ultimately results into prompting the cell's mechanism to begin the formation of new vasculature. With this acquired ability, the tumor cell can invade its surroundings to begin the growth of a secondary tumor and continue its malignancy. Once angiogenesis has commenced in tumor cells, nutrients can be supplied to these cells and their waste products removed. Cancer cells can also use these blood vessels to metastasize and pass through the blood vessels to distant sites where they can implant to start the growth of a new tumor. With this concurring metastasis, secondary tumor cells will need to develop their own ways of proliferation. In low oxygen conditions, tumor cells utilize anaerobic glycolysis to produce energy. Because of the low concentration of ATP that is produced using this cycle, tumor cells compensate by increasing glucose uptake through the increase of the production of glucose transporters such as GLUT1.[8]

1.3 Chemo and Radiotherapy Resistance of Tumor Cells

Hypoxia in tumor cells has been shown to be a contributor to chemo and radioresistance. A factor that contributes to chemoresistance of tumor cells is the apparent pH changes that occur within the environment of the cells. It was previously thought that hypoxia and acidosis in tumor cells concomitantly occur because of the lactate produced when oxidative phosphorylation gets switched to anaerobic glycolysis; but this is not the case.[11] It was shown that when tumor cells in hypoxic conditions are subjected to both buffered and non-buffered media, the cells survived in the buffered medium and the cells induced apoptosis in the non-buffered medium. One can infer from this study, therefore, that in hypoxic cells that are not experiencing acidosis, tumor cells can survive freely and have advantage over

healthy cells since programmed cell death would not commence.[12] Most anti-cancer drugs that are on the market require molecular oxygen to function. Drugs such as melphalan, an antitumor alkylating agent, have a higher chance of permeating the tumor cells and interacting with their DNA under normoxic conditions rather than a hypoxic tumor cell.[13] This phenomenon was seen when tumor cells were introduced into hypoxic conditions with drugs such as doxorubicin, another widely used anticancer drug. When doxorubicin was introduced to both normoxic and hypoxic tumor cells, the survival rate of the latter was increased.[13] Furthermore, when cancer cells experience acidosis, their microenvironment becomes an area where cellular uptake of drugs is decreased. The acidic extracellular environment of cancer cells contributes to chemoresistance due to some anticancer drugs having a weakly basic character (i.e. doxorubicin, mitoxantrone, vincristine and vinblastine).[14] As mentioned earlier, cancer cells have abnormal vasculatures and as such, there is limited blood flow to most areas in the cell that experiences hypoxia. Because of this, nutrients and drugs find it hard to reach these sites and thus contribute to chemoresistance.[14]

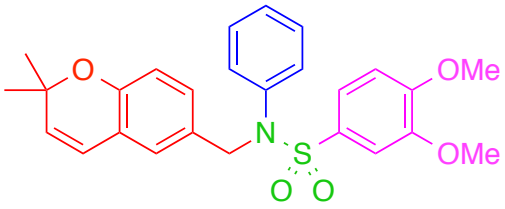
Another common way to treat cancer is through the use of radiotherapy. Radiotherapy does damage to tumor cells through induction of oxidative stress. When a malignant cancer cell is irradiated, either the DNA molecule itself or its environment that contains water molecule produce reactive oxygen species (ROS) that induce oxidative stress in the cell that can lead to DNA damage.[15] However, upon radiation and production of ROS, a study found that radiation itself induced HIF-1 activity in the tumor cells that led to the expression of VEGF and basic fibrolast growth factor (bFGF) that enhances endothelial cell radioresistance.[16]

Because of these reasons, the HIF-1 complex is a very attractive target for cancer therapy.

1.4 HIF-1 Inhibitors

Throughout the years since its discovery and evident route for anticancer therapy, many have pursued HIF-1 complex inhibitors. Most of the advances in this endeavor have been focused on the synthesis of small molecules that inhibit the HIF-1 pathway. Many of the therapeutic candidates that have been synthesized and are currently in preclinical studies have the target of altering the concentration of the HIF-1α subunit by interfering with its translation, degradation or its transcriptional activity.[17] One of the major subclasses of HIF-1 inhibitors consists mainly of heterocycle-based inhibitors that are derived from natural products.

To start this project, the laboratory of Dr. Erwin Van Mein in Emory University started the search for a small-molecule that shows potential HIF-1 complex inhibition using combinatorial chemistry. Some 10,000 compounds were screened from a 2,2-dimethylbenzopyran library. The chosen compounds were tested against human glioma cells that were transfected with an HRE-alkaline phosphatase reporter gene to measure their IC_{50} values.[6] From this library, a potential inhibitor, KCN-1 (Figure 3), was found, and was proven to be efficacious in inhibiting cancer growth.[18]



IC_{50}: 0.59 μM
cLogP: 5.20

Figure 3 Molecular structure of KCN-1

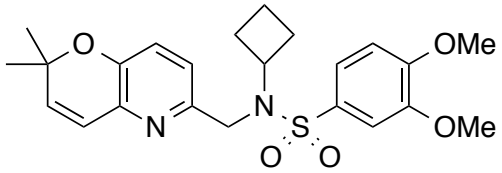
Although most HIF-inhibitors on the market affect the HIF-1α subunit by way of the HIF-1α's concentration in the cell, KCN-1 was seen to affect the complex differently.

Through mechanistic studies, it was seen that KCN-1 interrupts the association of the HIF-1α /HIF-1β heterodimer from its interaction with its co-activators p300/CBP.[6] This insight could lead to the synthesis of HIF-inhibitors that affect the HIF-1 complex through a different pathway.

2. DESIGN AND STRUCTURE OF INHIBITORS

2.1 KCN-1 Analogues

The main goal of the project was to synthesize more potent KCN-1 analogues with low to no toxicity. As seen in Figure 3, KCN-1 was divided into four regions for analogue synthesis: the benzopyran moiety (red), the nitrogen linker (blue), the sulfonamide moiety (green) and finally, the dimethoxy moiety (purple). Most of the changes done in this study were mostly focused on altering the nitrogen linker and the dimethoxy moiety in the hopes of synthesizing a more potent compound. Within this class, the most potent HIF-1 inhibitor previously synthesized by our group had an IC_{50} of 0.25 μM (SRIV-64b, Figure 4) and was tested against KCN-1, showing a threefold increase in potency.[6] With this lead, the synthesis of new HIF-1 sulfonamide analogues commenced.

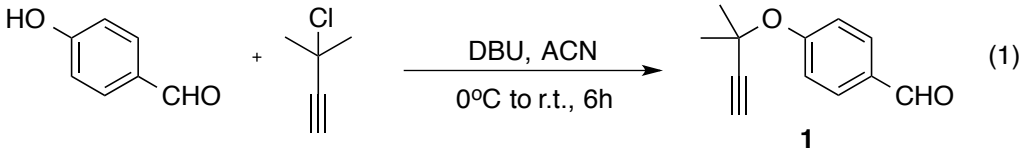


IC_{50}: 0.28μM
cLogP: 3.53

Figure 4 Molecular structure of SRIV-64b

2.1.1 Chemistry of Sulfonamide Analogues

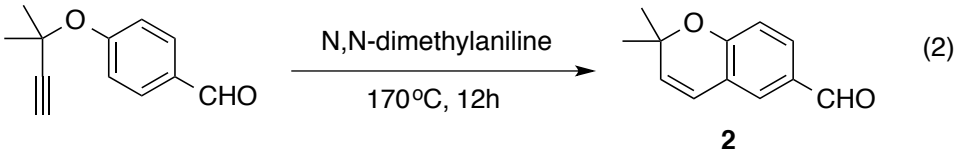
The synthesis of such compounds started with the benzopyran moiety. With a hydroxyaryl aldehyde and a tertiary alkyl halide as a starting material, the two compounds were condensed in the presence of a non-nucleophilic base such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in an SN1 fashion (Equation 1).



(1)

1

After this step, the cyclization of the ring occurred by subjecting the condensed product to basic conditions at 170 ^{o}C. (Equation 2).



(2)

2

This ring closure is afforded through a Claisen rearrangement whose mechanism is shown in Figure 5. Once the allene moiety is formed, the oxyanion attacked the sp^2 carbon to form the benzopyran moiety. However, the oxyanion could have attacked the sp carbon of the allene to form a benzofuran ring. The preference of the reaction to form the benzopyran ring can be rationalized by the angle of attack by the nucleophile.

Reaction Mechanism:

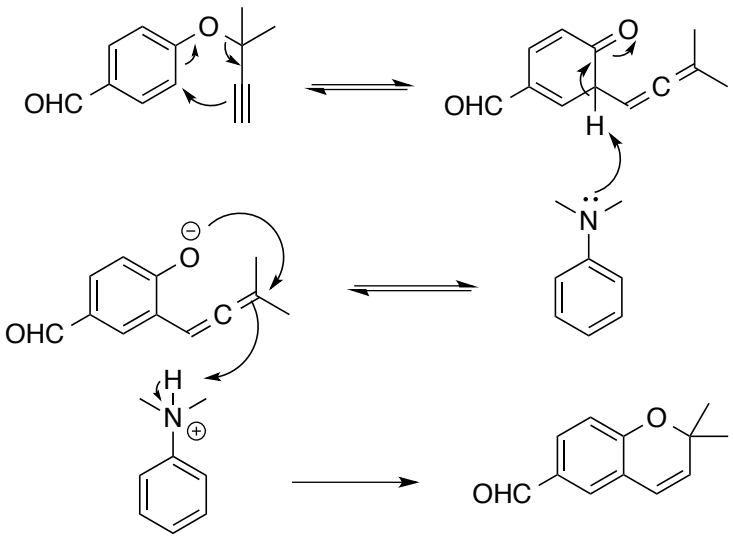


Figure 5 Mechanism of the Claisen rearrangement to close the benzopyran ring

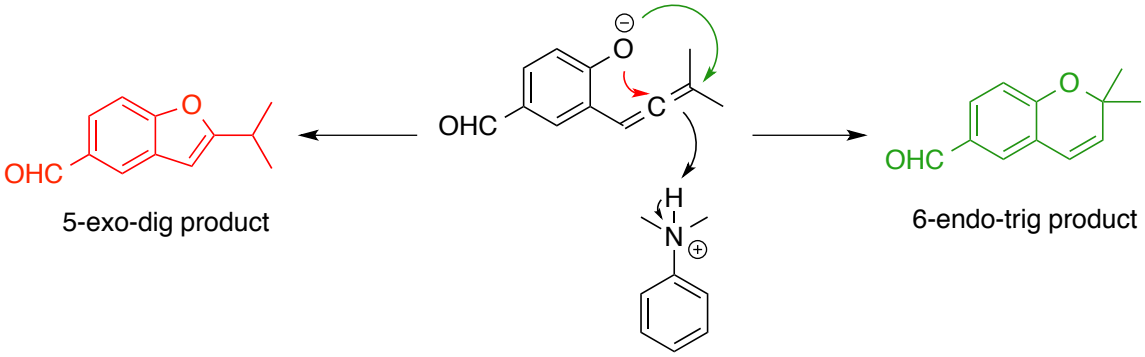
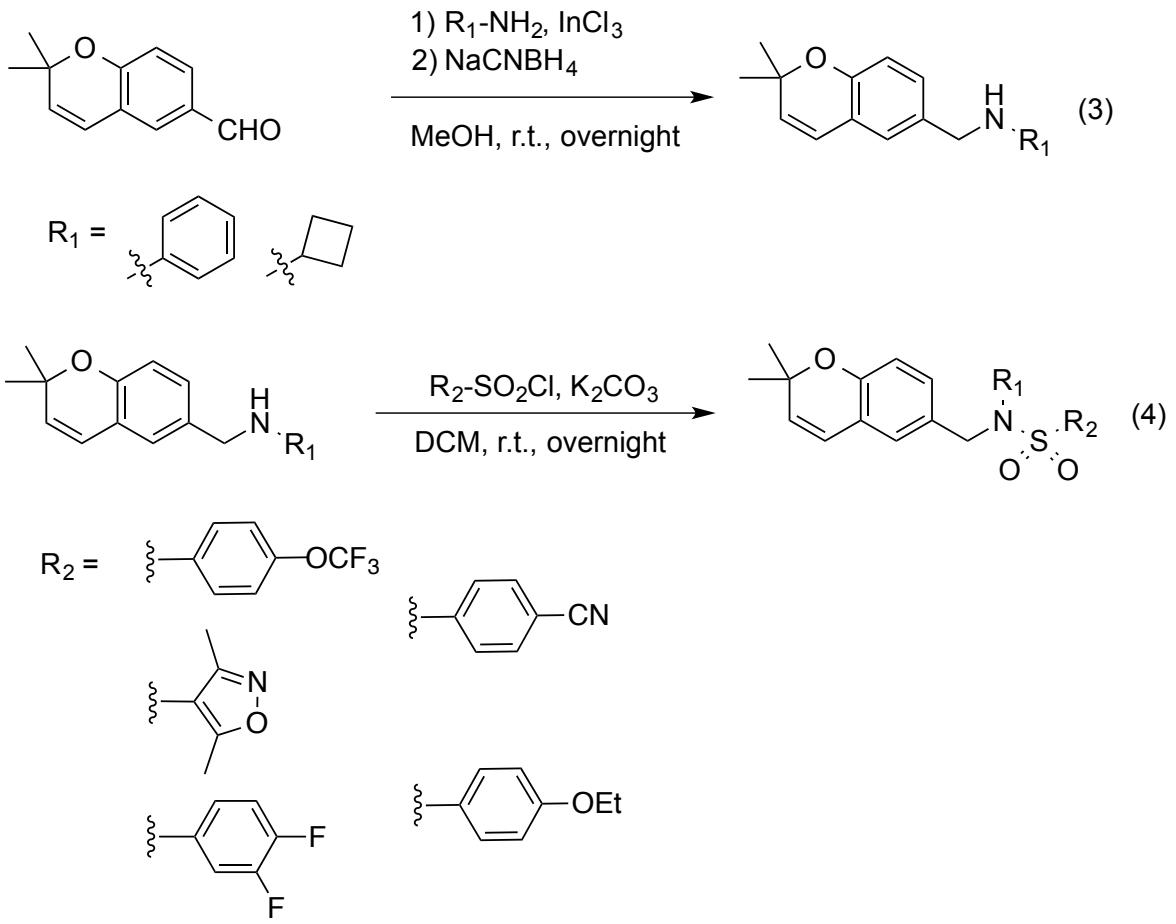


Figure 6 Two possible products from the Claisen rearrangement

If one were to analyze this mechanism using Baldwin's rules of ring closure, it can be seen that both products shown in Figure 6 could form. However, if the orientation between the oxyanion nucleophile and the electrophilic allene carbon were to be considered, the main reason as to why the formation of the benzopyran path (green) is favored over its counterpart is probably due to the angle from which it attacked the electrophile and how the dimethyl group faced the anionic specie. The dimethyl group was orthogonal to the sp-carbon in this case, which exposed the terminal carbon (sp^2) of the allene more to a nucleophilic attack.

After the synthesis of the left hand core, the nitrogen linker was introduced by reacting either an aliphatic or aromatic primary amine with the aldehyde to produce a secondary amine through reductive amination (Equation 3). The chosen nitrogen moieties for this scaffold in this study were aniline and cyclobutylamine (scaffolds for KCN-1 (X = C) and SR-IV-64b (X = N) respectively). Once the secondary amine had been formed, the next step was the introduction of the sulfonyl moiety by a sulfonylation reaction (Equation 4).



Scheme 1 Reductive amination and sulfonylation reaction with the different substitutions made on the scaffold

Different sulfonylation reactions were done to produce a variety of sulfonamide analogues (Scheme 1). The main group that was focused on in this scaffold was the

right hand core (sulfonyl moiety) to diversify the SAR studies done of previous analogues.

2.2 Structure Activity Relationships (SAR) of Previously Synthesized Analogues[a]

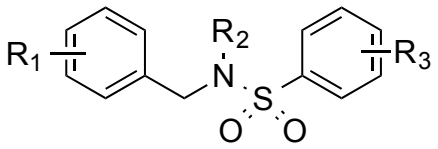


Figure 7 General scaffold of sulfonamide analogues

As seen in Figure 7, the analogues synthesized follow a general scaffold in this study. The previous SAR profile demonstrated that on the left hand core, benzopyrans and pyrano [3,2b] pyridines showed an increase in inhibition activity. Although other fused rings are tolerated, it did not show an increase in potency as compared to KCN-1. The geminal dimethyl moiety on both the benzopyran and pyridinyl rings also showed significance since their loss in the scaffold led to a decrease in activity. For the nitrogen linker, the activity was at its best when the substituents on the nitrogen were an aromatic ring and cycloalkyl rings of less than 6-carbons in size; furthermore, it was seen that short alkyl chains were tolerated as well. It was also generally seen that the sulfonamide group itself (N-SO_2) was crucial for biological inhibition. Lastly, for the right hand core, it was seen that the activity was more pronounced if an aromatic group was present that had substituents on the *para* position as opposed to *meta* substituted aromatic rings.[6] In choosing the variation that were to be made with the compounds, the Lipinski's Rule of Five was

[a] All of the SAR studies were obtained from Dr. Suazette Mooring's studies.[6]

selected to be the criteria to be followed. This allowed our group to synthesize compounds that followed general rules when considering what functional groups that were chosen to be introduced into the new analogues.

2.3 Manassantin B Scaffold

During the course of this project, about 200 compounds have been synthesized by our group. This library consists purely of sulfonamide analogues and only about 20% of the compounds in the library were active. In the hopes of finding a much more potent candidate of HIF-1 inhibitors, new scaffolds were being investigated as a potential HIF-1 inhibitors.

Manassantin B, a natural product that is extracted from the plant *Saururus cernuus* (common name: lizard's tail) along with another extract, 4-*O*-demethylmanassantin have been discovered to affect the HIF-1 complex and inhibit its activity with IC_{50} values in the range of 3 and 30 nM respectively.[19]

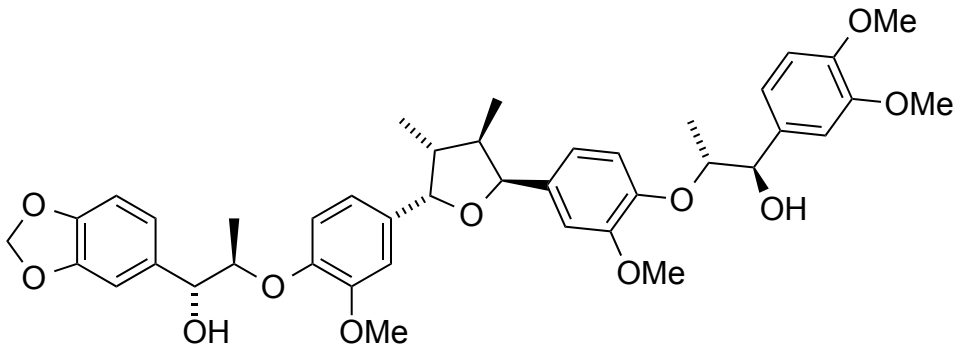


Figure 8 Molecular structure of Manassantin B

Manassantin B and 4-*O*-demethylmanassantin only differ by one methoxy group on the right hand side of the molecule; however, studies show that this slight change gives Manassantin B a tenfold increase in its potency in inhibiting the HIF-1 activity.[19]

With this knowledge in hand, the synthesis of analogues that followed this scaffold commenced. The structure of Manassantin B is very complex; it would have been very tedious if synthesis of a very similar analogue were to be done solely for trial purposes. If the structure were taken into consideration, there is a relative similarity between the left side and the right side of the molecule that is only separated by a furan ring. Therefore, it was decided to direct the synthesis of analogues towards creating compounds that looked similar to one side of the natural product.

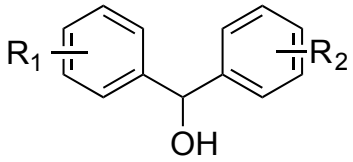
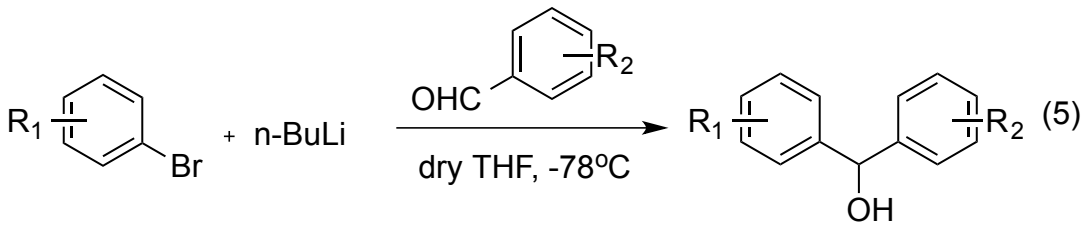


Figure 9 Simplified structure of scaffold based on Manassantin B

2.3.1 Chemistry of Manassantin B-like analogues

Looking at the general structure shown in Figure 9, there are three structural groups that are important in this scaffold: the left core, the right core, and the hydroxymethine moiety. Different substitutions can be made with both left and right cores to see if they affect the HIF-1 complex as effectively as the natural product. The chemistry of these analogues usually starts with the preparation of both aryl groups (left and right core) separately before combining them (Equation 5). One of the aryl groups is usually prepared as a substituted aryl bromide and the other aryl group is usually prepared as a substituted aryl aldehyde. These two groups are condensed using n-butyllithium under an inert atmosphere at -78^{o}C as seen in Equation 5.



Equation 5 Condensation of the two cores for Manassantin-B derived analogues. R_1 and R_2 groups are listed in Figure 10

2.4 Biological testing of analogues

After the synthesis of the HIF-1 inhibitors, our collaborators at the Van Meir laboratory performed the biological testing of the analogues to investigate their HIF-1-inhibiting activity. Using the plasmid construct with the six copies of the HRE of the VEGF gene that are upstream of a luciferase reporter gene, the IC_{50} of each analogue was reported using a concentration curve at 0, 1, 2, 3 and 5 μM with SR-IV-64b (Fig. 4) as a standard to compare the IC_{50} values to. In the results section of this study, any analogue that showed activity beyond 5 μM were not further tested and was designated to have activities >5 μM. These compounds' activities were not further evaluated and thus their exact inhibiting activity, or lack thereof, was unknown. Furthermore, the IC_{50} value of SR-IV-64b was not constant and had a range of 0.28 ± 0.12 μM in various experiments.

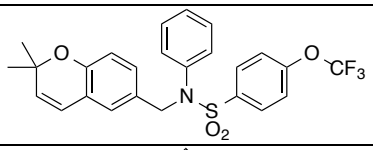
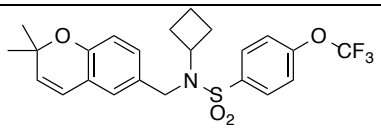
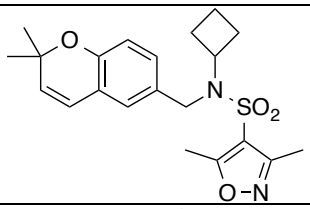
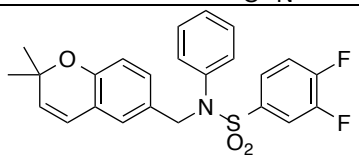
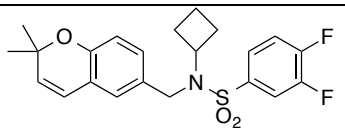
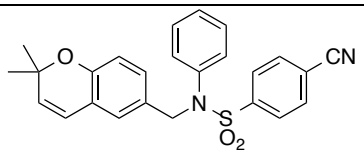
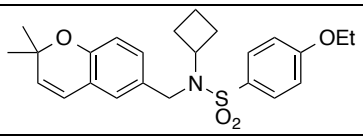
3. RESULTS AND DISCUSSION

3.1 Sulfonamide Analogues

Using the SAR profile that was generated from previous studies, a couple of new analogues were synthesized. The main variation that was done on these analogues

targeted the nitrogen linker and the right hand core. The left hand core kept the 2,2-dimethylbenzopyran group and the sulfonamide group was also retained. Below is the table of the sulfonamide analogues synthesized with their corresponding IC_{50} and calculated LogP values which is the partition coefficient between hydrophobic and hydrophilic media.[b,20]

Table 3 List of sulfonamide analogues synthesized with the 2,2-dimethylbenzopyran moiety kept intact

Compound	Structure	Mol. Wt. (g/mol)	cLogP	IC_{50} (μM)
3		489.12	3.74	>5
4		467.14	3.80	>5
5		402.51	2.51	>5
6		441.12	2.92	>5
7		419.14	3.24	>5
8		430.14	2.48	>5
9		427.18	3.22	4.37

[b] All LogP values were calculated using a virtual computational chemistry program. (VCCLAB, Virtual Computational Chemistry Laboratory, http://www.vcclab.org, 2005.)

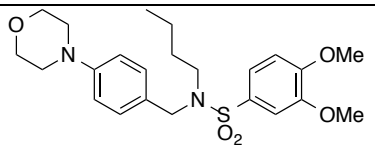
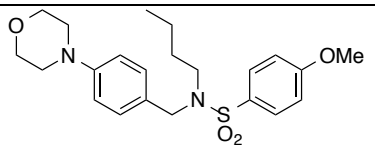
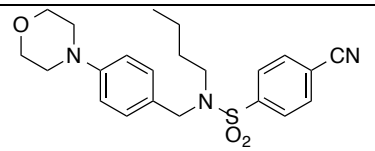
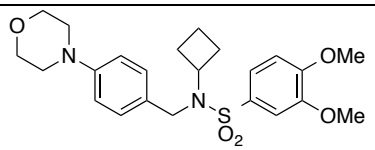
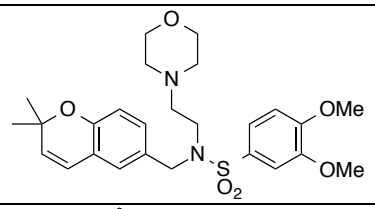
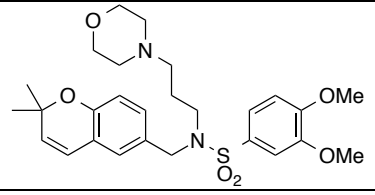
With the series of compounds synthesized and comparing it to KCN-1 and SRIV-64b, it can be seen that there was a decrease in biological activity once the right hand core was changed. Thus, it can be generalized that the dimethoxy group on both the *para* and *meta* positions of the aromatic ring on the sulfonamide analogues are necessary for biological activity. Of all the analogues that were synthesized in this class, only compound **9** was seen to remotely inhibit the activity of the HIF-1 complex. This also proves that the dimethoxy group on the right hand is arguably a required group for biological inhibition since compound **9** is the only compound in the group that remotely resembles the active analogue (Figure 4). Furthermore, it can also be noted that although almost all analogues synthesized were inactive, all of them had cLogP values that were less than five, which is considered to be the upper limit of desired lipophilicity based on Lipinski's Rule of Five that was used throughout this study.

3.1.1 Morpholine group introduction

Another approach that was taken during this study was the introduction of other ring structures into the sulfonamide group. For this particular study, we were hoping that the introduction of the morpholine group into our compounds would improve the analogues' aqueous solubility while maintaining potency without introducing any further cellular toxicity. The chemistry of the analogues synthesized with this group followed the same procedures that were mentioned previously. This procedure used 4-morpholinylbenzaldehyde as a starting material rather than its chromene counterpart (Scheme 1). The morpholine moiety was both introduced into the left hand core of the scaffold as well as the nitrogen linkers. The analogues were

subjected to same biological testing, and their IC_{50} values were measured and LogP calculated.

Table 4 List of sulfonamide analogues synthesized with morpholine groups

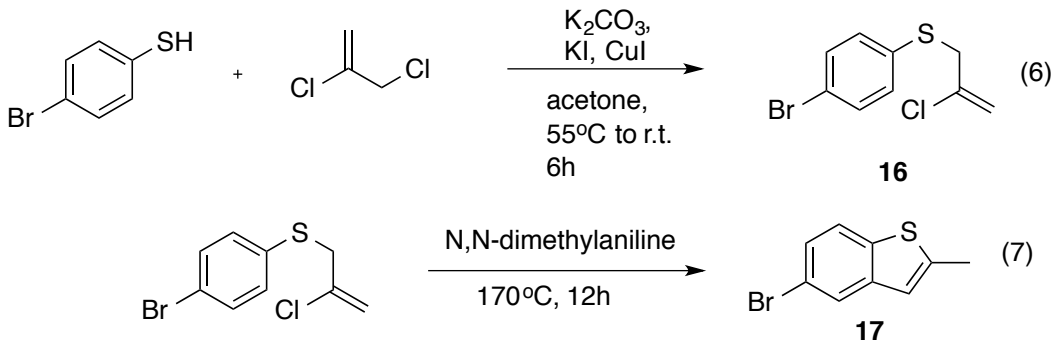
Compound	Structure	Mol. Wt.	cLogP	IC_{50} (μM)
10		448.20	3.51	1.23
11		418.19	3.41	>5
12		413.18	2.97	>5
13		446.19	3.33	2.62
14		502.21	3.13	>5
15		516.23	3.50	>5

Looking at Table 4, the first change that was made was to introduce the morpholine ring into the left hand core of the scaffold. This was done in conjunction with the nitrogen linker having either a cyclobutyl or n-butyl substituent on the nitrogen atom (compounds **10**-**13**). From this set, it can be seen that although the calculated LogP is comparably the same with the first set of sulfonamides synthesized, this set of analogues were relatively more active. This biological activity was perhaps caused by the combination of the morpholine group in tandem with an aliphatic nitrogen

linker. The next change that was made in the scaffold was to introduce the morpholine group into the nitrogen linker and keep the 2,2-dimethylbenzopyran and dimethoxybenzyl group with the right hand and left hand core. As seen in Table 4, by introducing the morpholine group, there was not much difference that was seen in solubility; however, it is notable that compounds **14** and **15** lost their activities when the morpholine group was introduced. As it was previously mentioned that the dimethoxy group was necessary for biological activity; therefore, the morpholine group was not introduced into the right hand core.

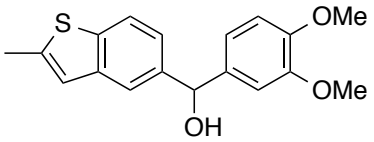
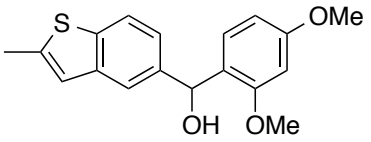
3.2 Manassantin-B derived Analogues

For the synthesis of Manassantin B-derived analogues, the focus of variation was first directed towards the right hand side of the molecule as can be seen in the two compounds that were synthesized in Table 5. These compounds contain a thioether ring that replaced the normal benzopyran group. This was done to diversify the compounds that were already synthesized. The synthesis of such compounds was done using the procedure described below.



Scheme 2 Reaction procedure to synthesize the aryl-sulfane and thiophene moieties

Table 5 Two analogues that were synthesized that followed the new scaffold

Compound	Structure	Mol. Wt.	cLogP	IC_{50} (μM)
18		314.10	4.18	1.03
19		314.10	4.11	>5

Looking at compounds **18** and **19**, one important observation can be made. The structural difference between Manassantin B and 4-*O*-demethylmanassantin was only one methoxy group at the *meta* position of Manassantin B. This difference gave a tenfold increase in potency to the said molecule. Reviewing the compounds in Table 5, it can be seen that even if the structure did not mirror the natural product, it is still very obvious that the compound lost its biological activity once the methoxy group on the *meta* position of the aryl was eliminated. This experiment gives a good starting point for the SAR profile on the right core since it proves how necessary the dimethoxy moiety is.

3.2.1 Importance of Hydroxymethine in the Scaffold

Variation was also done on this new scaffold by changing the hydroxymethine group of the molecule. The efforts to change the group on the left hand side of the molecule have been substantial and our group has developed analogues that have very promising IC_{50} values. Therefore, for this particular study, it was decided to shift the focus to the hydroxymethine group and to observe its activity once it was changed based off of analogues that were previously synthesized. Five analogues whose variation was mainly focused on the left hand ring were chosen to see if their activity would change once the hydroxymethine group was varied. With this scaffold,

only the hydroxymethine group was changed and the right core of the analogues contained the dimethoxy groups in the *para* and *meta* positions of the aromatic ring. These five analogues were chosen as base compounds since they were either active as sulfonamide or as Manassantin B-like compounds. By oxidizing the hydroxy group into ketones using pyridinium chlorochromate, their activities were observed to see if any changes in the hydroxymethine group were significant enough in the gain or loss of biological inhibition.

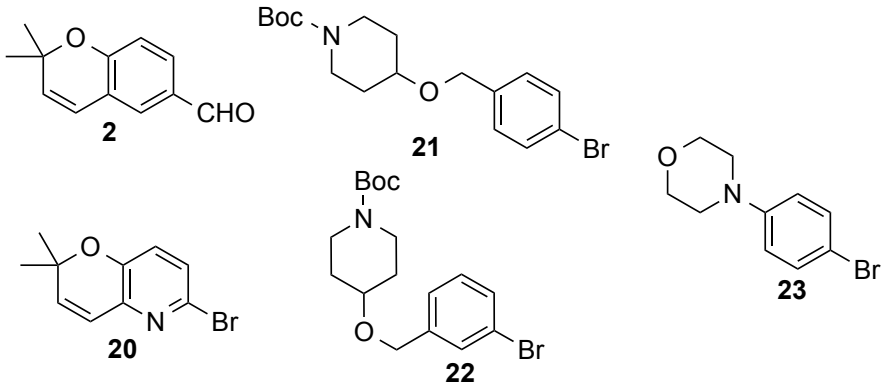
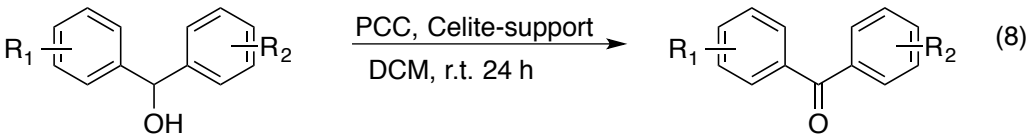


Figure 10 Functionalities of the five precursors chosen for hydroxymethine variation. These precursors were then reacted with either the 4-bromobenzene or 4-bromobenzaldehyde to produce their hydroxymethine compounds.

The oxidation of the hydroxymethine group into its ketone counterpart was done using PCC oxidation and is described in Equation 8.



(8)

Moreover, the hydroxymethine compounds that were used to synthesize the ketone products are listed below.

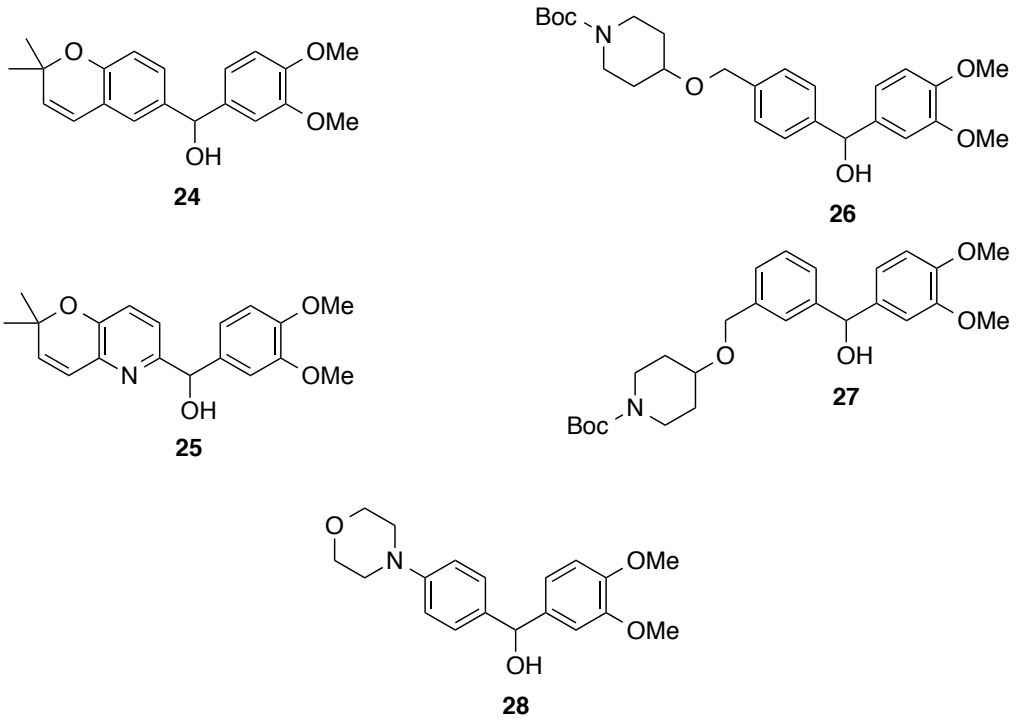
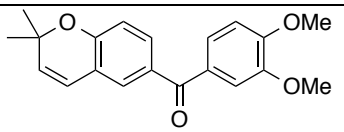
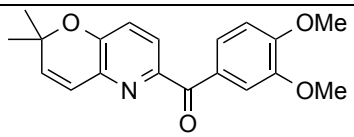
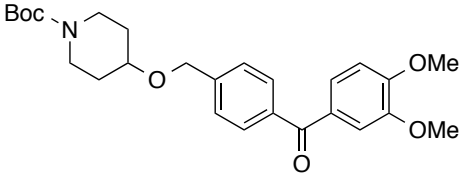
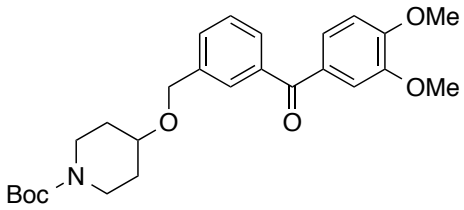
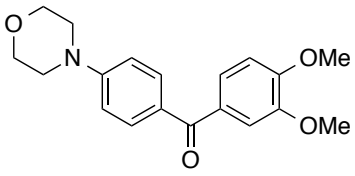


Figure 11 List of hydroxymethine compounds used to make the ketone products.

In Figure 11, the figures for the five analogues whose left core was varied are drawn. The summary of their activities and their respective cLogP values are listed in Table 6.

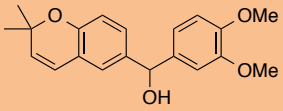
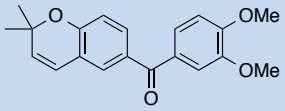
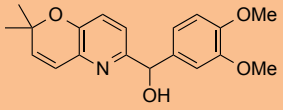
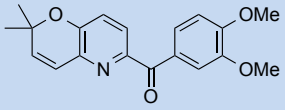
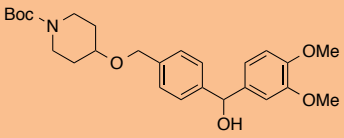
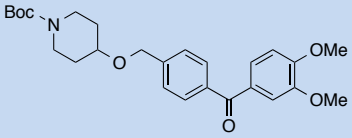
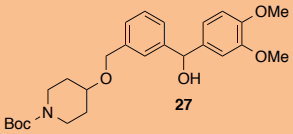
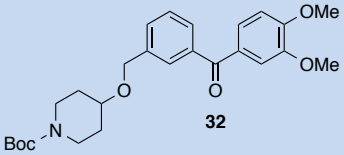
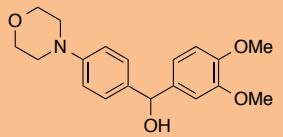
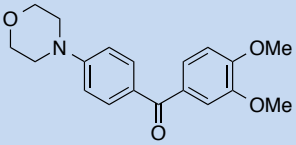
Table 6 Biological results for the ketone analogues

Compound	Structure	Mol. Wt.	cLogP	IC_{50} (μM)
29		324.14	4.36	>5
30		325.36	3.49	>5
31		455.23	4.05	4.50
32		455.23	4.02	>5

33		327.15	3.06	>5

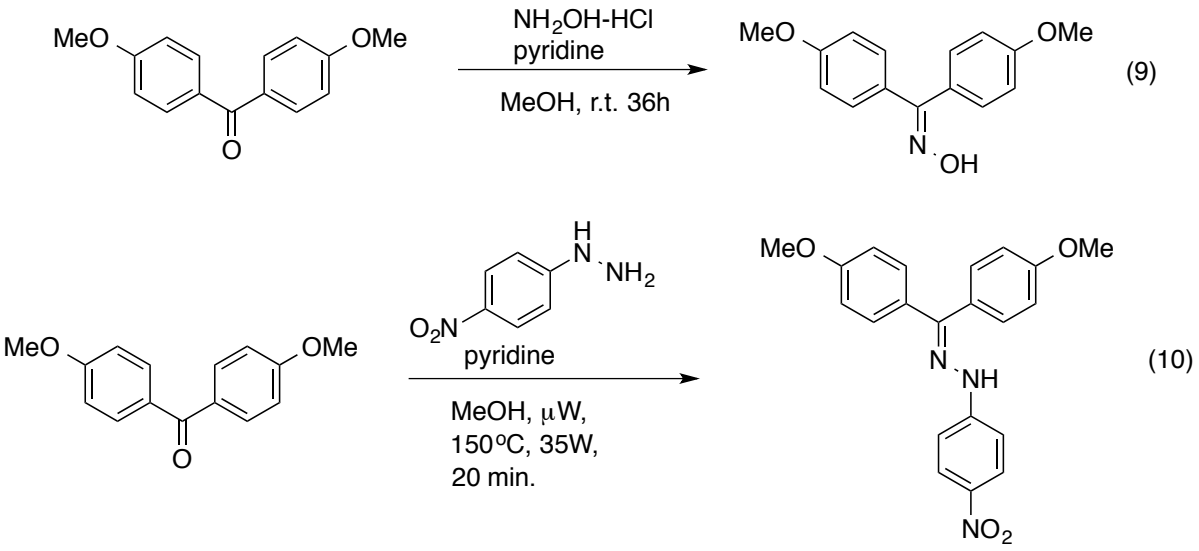
As seen in Table 6 and the comparison that was made in Table 7 below, it is obvious that the hydroxyl group on the hydroxymethine carbon proved to be highly important since its elimination led to a complete depletion of HIF-1 activity, as clearly seen in the case of the most potent compound in the list, compound **32**. This result gives a clear view of what future directions to take and focus can be directed on the left core of the molecule.

Table 7 Comparison of the data obtained for the hydroxymethine and ketone analogues

Compound	IC_{50} (μM)	cLogP	Compound	IC_{50} (μM)	cLogP
 **24**	>5	4.23	 **29**	>5	4.36
 **25**	2.25	3.47	 **30**	>5	3.49
 **26**	0.89	3.55	 **31**	4.50	4.05
 **27**	0.20	3.52	 **32**	>5	4.02
 **28**	>5	2.63	 **33**	>5	3.06

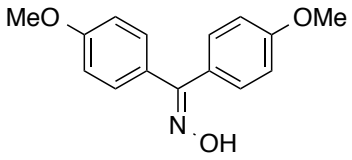
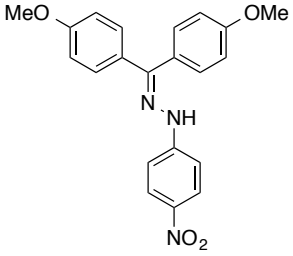
3.2.2 Miscellaneous Compounds

In the hopes of further diversifying the library of the new scaffold, two compounds were made to test synthetic procedures that would mimic the reactions that were planned for the ketone moieties synthesized. The carbonyl group of the ketones synthesized was reacted with hydroxylamine and hydrazine to form the oxime and hydrazone groups respectively. These compounds, albeit slightly different from the original scaffold, were submitted for biological testing to observe their activity. The compounds are listed in Table 7 and their respective reaction procedures can be seen below.



Scheme 3 Reaction procedures for the synthesis of the miscellaneous compounds

Table 8 Miscellaneous compounds synthesized for synthetic purposes

Compound	Structure	Mol. Wt.	cLogP	IC_{50} (μM)
34		257.11	3.19	>5
35		377.14	5.31	>5

The two compounds that are seen in Table 7 were found to be inactive towards HIF-1 inhibition. However, the synthetic procedures that were used to make such compounds were successful and can be used to create new analogues that contain the oxime and hydrazone moieties.

4. Conclusion and Future Direction

Cancer has been plaguing humanity since the earliest records of medicine were made. Although medical advances have contributed immensely to the search for a good therapy to cure cancer, it is still a challenge for scientists to improve treatments by decreasing the therapies' side effects while increase potency. The HIF-1 complex is a very attractive target for cancer therapy because of its role in tumor biology. Its role as an angiogenetic promoter, among other things, can be exploited to create small molecules that would inhibit a tumor's function and thereby inhibiting progression of cancer cells. In this study, a total of 22 compounds were synthesized that fell on three different classes of compounds. Most of the compounds that were synthesized in this study included sulfonamide analogues that give further diversity

with to the previously created library and will further elucidate the SAR profile of the sulfonamide class of HIF-1 inhibitors we have studied thus far. Some compounds were also synthesized that were based off of Manassantin B and have given us a new scaffold to investigate for HIF-1 inhibition. The last class of compounds that was synthesized were analogues of a potent Manassantin B-derived compound previously synthesized by other members of our group. These compounds proved that the hydroxymethine group in this particular scaffold holds great importance since its elimination leads to loss of inhibition. In the future, the observations made through this study will help in the synthesis of new and more potent HIF-1 inhibitors.

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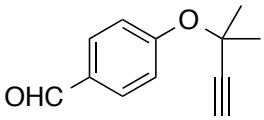
Experimental:

All starting materials were obtained from Sigma-Aldrich, Acros Organics or Oakwood Chemicals and were used without further purification. Microwave heating was performed in a single-mode microwave cavity of a Discovery Synthesis System (CEM corp.) and the microwave-irradiated reactions were conducted in a heavy-walled glass vials sealed with Teflon septa. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively, on a Bruker Avance 400 NMR spectrometer using $CDCl_3$ containing tetramethylsilane (TMS) an internal calibration standard. Mass spectra analyses were performed by the mass spectrometry facilities at Georgia State University.

Procedures:

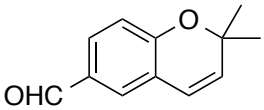
I. Sulfonamide analogues



4-((2-Methylbut-3-yn-2-yl)oxy)benzaldehyde (1)

In a 100 mL round bottom flask, 2 g (0.015 mol) of p-hydroxybenzaldehyde was dissolved in dry acetonitrile (10 mL) and was cooled to 0 ^{o}C under inert atmosphere with argon gas. To this solution, 9.0 mL (0.06 mol) of DBU was added and the solution was allowed to stir for 30 min. 6.8 mL (0.06 mol) of 3-chloro-3-methylbut-1-yne was then added into the mixture drop wise. The solution was allowed to warm up to room temperature and was stirred overnight. The solution was concentrated and extracted with ethyl acetate (100 mL). The organic solution was washed with 1M HCl

solution (20 mL), 1M NaOH solution (20 mL), saturated $NaHCO_3$ solution (20 mL), and brine (20 mL) and was dried over Na_2SO_4. The organic layer was concentrated in vacuo and was taken directly to the next step.



2,2-Dimethyl-2*H*-chromene-6-carbaldehyde (2)

Using the impure product from the procedure above, the crude mixture was dissolved in *N*,*N*-dimethylaniline (<1 mL) and heated at 170 ^{o}C for 6 h. After cooling to room temperature, the organic layer was extracted with ethyl acetate (20 mL), and washed with IM HCl (20 mL x 3), saturated $NaHCO_3$ solution (20 mL), and brine 20 mL), and was dried over Na_2SO_4. The organic layer was concentrated in vacuo. The product was purified using flash column chromatography. Ethyl acetate and hexanes were used as eluent (1:8). Yield: 2 g, 37%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (s, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.28 (s, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 6.14 (d, *J* = 8.0 Hz, 1H), 5.47 (d, *J* = 8.0 Hz, 1H), 1.24 (s, 6H) ppm. ^{13}C NMR: δ 190.2, 158.3, 131.5, 131.3, 129.9, 127.7, 121.2, 121.0, 116.7 and 28.24 ppm.

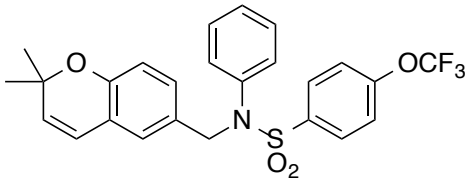
General procedure for the reductive amination of 2,2-dimethyl-2*H*-chromene-6-carbaldehyde:

To a solution of 100 mg of aldehyde (1 eq.) and 21 mg of $InCl_3$ (0.15 eq.) in dry MeOH (10 mL) under Argon gas, the corresponding amount of amine (1.5 eq.) was added. The mixture was allowed to stir until completion as monitored by TLC. Upon consumption of the aldehyde, 36 mg of $NaCNBH_4$ (1.5 eq.) was added and was allowed to stir for 1 h. The reaction mixture was quenched with saturated 10 mL of

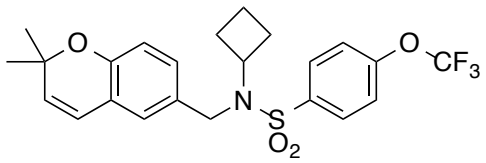
NH_4Cl solution. The organic layer was extracted with ethyl acetate (20 mL), washed with brine (20 mL) and dried over Na_2SO_4. The product was taken to the next step without further purification.

General procedure for sulfonylation reactions of the secondary amine:

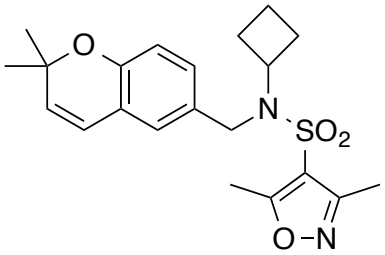
In a 50 mL round-bottom flask, 50 mg of the crude secondary amine (1 eq.) in DCM (10 mL) was added the corresponding amounts of K_2CO_3 (2 eq.), then appropriate amounts of the sulfonyl chloride moiety (2 eq.). The reaction mixture was stirred at room temperature for 24 h. The solution was then washed with deionized water (10 mL) and the organic layer was extracted with DCM (10 mL x 2), washed with brine (20 mL), dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified using flash column chromatography. Ethyl acetate and hexanes were used as eluent (1:8).



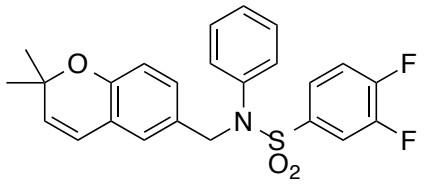
***N*-((2,2-Dimethyl-2*H*-chromen-6-yl)methyl)-*N*-phenyl-4-(trifluoromethoxy)benzenesulfonamide (3) –** Yield: 18 mg, 18%. ^{1}H NMR: δ 8.13-8.11 (d, *J* = 8.8 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.8 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.23-7.22 (m, 2H), 6.96 (d, *J* = 3.2 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 6.22 (d, *J* = 10.0 Hz, 1H), 5.57 (d, *J* = 10.0 Hz, 1H), 4.63 (s, 2H), 1.38 (s, 6H) ppm. ^{13}C NMR: δ 138.6, 137.3, 131.0, 129.8, 129.5, 129.4, 129.1, 129.0, 128.1, 127.7, 126.7, 122.0, 121.2, 121.1, 120.6, 116.1, 54.6, 28.0 ppm. HRMS (ESI) *m/z* calculated for $C_{25}H_{22}F_3NO_4S + Na^+$: 512.1119, found 512.1106.



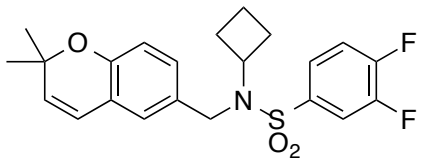
***N*-Cyclobutyl-*N*-((2,2-dimethyl-2*H*-chromen-6-yl)methyl)-4-(trifluoromethoxy)benzenesulfonamide (4)** – Yield: 66 mg, 48%. ^{1}H NMR: δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.96 (s, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 6.30 (d, *J* = 9.6 Hz, 1H), 5.63 (d, *J* = 9.6 Hz, 1H), 4.33 (s, 2H), 4.26-4.18 (m, 1H), 2.03-1.99 (m, 4H), 1.58 (m, 2H), 1.44 (s, 6H) ppm. ^{13}C NMR: δ 152.3, 151.9, 139.0, 131.1, 129.9, 129.1, 127.9, 125.3, 122.2, 121.3, 120.8, 116.2, 52.9, 48.2, 29.3, 28.0, 15.0 ppm. HRMS (ESI) *m/z* calculated for $C_{23}H_{24}NO_4F_3S$ + Na^+: 490.1276, found 490.1278.



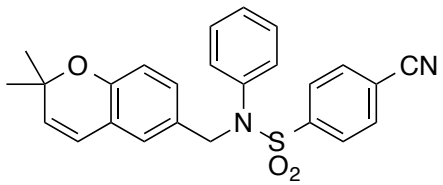
***N*-Cyclobutyl-*N*-((2,2-dimethyl-2*H*-chromen-6-yl)methyl)-3,5-dimethylisoxazole-4-sulfonamide (5)** - Yield: 47 mg, 43%. ^{1}H NMR: δ 7.02 (d, *J* = 8.4 Hz, 1H), 6.91 (s, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.31-6.28 (d, *J* = 10.0 Hz, 1H), 5.65-5.62 (d, *J* = 10.0 Hz, 1H), 4.41 (s, 2H), 4.28-4.10 (m, 1H), 2.58 (s, 3H), 2.39 (s, 3H) 2.09-2.04 (m, 4H), 1.62-1.52 (m, 2H) 1.43 (s, 6H) ppm. ^{13}C NMR: δ 172.7, 157.3, 152.4, 131.3, 129.5, 127.8, 125.2, 122.1, 121.4, 117.5, 116.3, 52.2, 47.8, 29.3, 27.9, 15.0, 12.8, 11.1 ppm. HRMS (ESI) *m/z* calculated for $C_{21}H_{26}N_2O_4S$ + Na^+: 425.1511, found 425.1529.



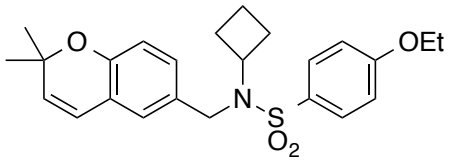
***N*-((2,2-Dimethyl-2*H*-chromen-6-yl)methyl)-3,4-difluoro-*N*-phenylbenzenesulfonamide (6)** - Yield: 30 mg, 37%. ^{1}H NMR: δ 7.50 (t, *J* = 8.8 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.32-7.26 (m, 4H), 6.98-6.96 (m, 2H), 6.89 (d, *J* = 10.8 Hz, 2H), 6.62 (d, *J* = 10.0 Hz, 1H), 6.24 (d, *J* = 10.0 Hz, 1H), 5.59 (d, *J* = 10.0 Hz, 1H), 4.65 (s, 2H), 1.41 (s, 6H) ppm. ^{13}C NMR: δ 152.6, 138.4, 131.0, 129.4, 129.1, 129.0, 128.3, 127.6, 126.7, 122.0, 121.2, 118.0, 117.8, 116.2 ppm. HRMS (ESI) *m/z* calculated for $C_{24}H_{21}NO_3F_2S$ + Na^+: 464.1108, found 464.1097.



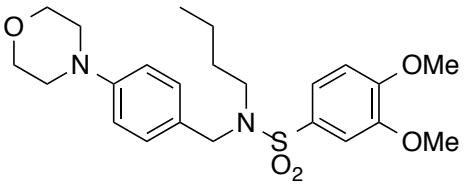
***N*-Cyclobutyl-*N*-((2,2-dimethyl-2*H*-chromen-6-yl)methyl)-3,4-difluorobenzenesulfonamide (7)** –Yield: 37 mg, 29%. ^{1}H NMR: δ 7.61-54 (m, 2H), 7.29-7.28 (m, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.96 (s, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 6.30 (d, *J* = 9.6 Hz, 1H), 5.64 (d, *J* = 9.6 Hz, 1H), 4.32 (s, 2H), 4.23-4.19 (m, 1H), 2.06-1.99 (m, 4H), 1.55-1.52 (m, 2H), 1.44 (s, 6H) ppm. ^{13}C NMR: δ 152.4, 148.9, 137.4, 131.1, 129.7, 128.0, 125.3, 122.1, 121.3, 118.1, 117.9, 117.0, 116.8, 116.3, 52.8, 48.2, 29.3, 28.0, 15.0 ppm. HRMS (ESI) *m/z* calculated for $C_{22}H_{23}NO_3F_2S$ + Na^+: 442.1264, found 442.1255.



4-Cyano-*N*-((2,2-dimethyl-2*H*-chromen-6-yl)methyl)-*N*-phenylbenzenesulfonamide (8) –Yield: 15 mg, 30%. ^{1}H NMR: δ 7.77 (q, *J* = 8.4 Hz, 4H), 7.27 (t, *J* = 5.2, 3H), 6.95-6.93 (m, 2H), 6.89-6.85 (m, 2H), 6.62 (d, *J* = 8.0 Hz, 1H), 6.23 (d, *J* = 10.0 Hz, 1H), 5.60 (d, *J* = 10.0 Hz, 1H), 4.66 (s, 2H), 1.41 (s, 6H) ppm. ^{13}C NMR: δ 152.7, 143.2, 138.2, 132.7, 131.1, 129.5, 129.2, 129.1, 128.4, 128.2, 127.3, 126.7, 122.0, 121.2, 116.3, 116.2, 54.9, 28.0 ppm. HRMS (ESI) *m/z* calculated for $C_{25}H_{22}N_2O_3S + Na^+$: 453.1249, found 453.1260.

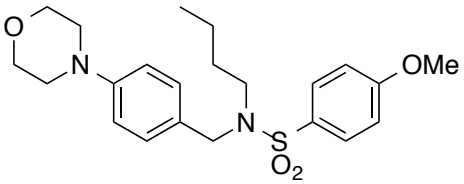


***N*-Cyclobutyl-*N*-((2,2-dimethyl-2*H*-chromen-6-yl)methyl)-4-ethoxybenzenesulfonamide (9)** – Yield: 16 mg, 36%. ^{1}H NMR: δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.98 (s, 1H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.29 (d, *J* = 10.0 Hz, 1H), 5.60 (d, *J* = 10.0 Hz, 1H), 4.26 (s, 2H), 4.18-4.10 (m, 1H), 4.10-4.05 (m, 2H), 2.00-1.90 (m, 4H), 1.52-1.44 (m, 5H), 1.42 (s, 6H) ppm. ^{13}C NMR: δ 162.1, 152.1, 131.8, 130.9, 130.7, 129.1, 127.9, 125.3, 122.4, 121.2, 116.1, 114.5, 63.9, 52.9, 48.2, 29.2, 28.0, 15.1, 14.6 ppm. HRMS (ESI) *m/z* calculated for $C_{24}H_{29}O_4NS + Na^+$: 450.1710, found 450.1709.

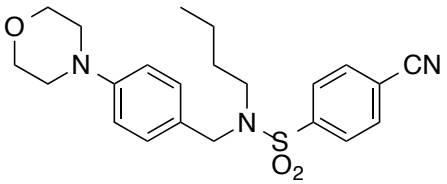


***N*-Butyl-3,4-dimethoxy-*N*-(4-morpholinobenzyl)benzenesulfonamide (10)** – Yield: 10 mg, 23%. ^{1}H NMR: δ 7.47 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 5.2 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 4.26 (s, 2H), 3.97 (s, 3H), 3.92 (s, 3H), 3.87 (t, *J* = 4.4. Hz, 4H), 3.16 (t, *J* = 9.2 Hz, 4H), 3.09 (t, *J* = 7.6 Hz, 2H), 1.39-1.34 (m, 2H), 1.32-26 (m, 2H), 1.18 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C

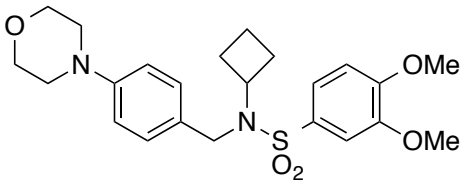
NMR: δ 152.3, 149.0, 132.2, 129.4, 121.0, 115.5, 110.6, 110.0, 66.9, 56.2, 51.0, 49.3, 47.3, 29.9, 19.9, 13.6 ppm. HRMS (ESI) *m/z* calculated for $C_{23}H_{33}N_2O_5S$ [(M + H)$^+$]: 449.2110, found 449.2094.



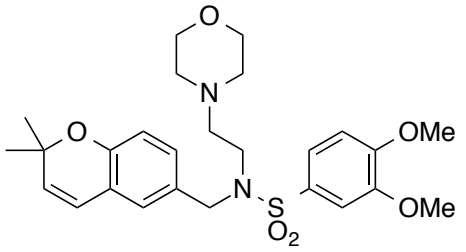
***N*-Butyl-4-methoxy-*N*-(4-morpholinobenzyl)benzenesulfonamide (11)** – Yield: 48 mg, 36%. ^{1}H NMR: δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 4.23 (s, 2H), 3.87-3.85 (m, 4H), 3.84 (s, 3H), 3.15-3.13 (m, 4H), 3.04 (t, *J* = 7.6 Hz, 2H), 1.35-1.27 (m, 2H), 1.17-1.09 (m, 2H), 0.76-0.72 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR: δ 162.6, 132.1, 129.4, 129.2, 115.6, 114.2, 66.9, 55.6, 51.1, 49.3, 47.3, 30.0, 19.9, 13.6 ppm. HRMS (ESI) *m/z* calculated for $C_{22}H_{31}O_4N_2S$ [(M + H)$^+$]: 419.1999, found 419.1980.



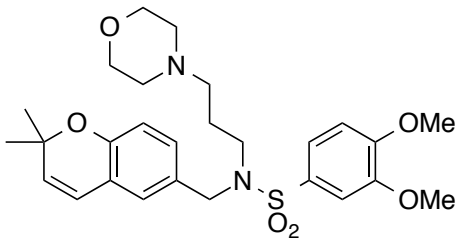
***N*-Butyl-4-cyano-*N*-(4-morpholinobenzyl)benzenesulfonamide (12)** – Yield: 21 mg, 33%. ^{1}H NMR: δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 8.4, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 4.31 (s, 2H), 3.89-3.86 (m, 4H), 3.17-3.11 (m, 6H), 1.38-1.34 (m, 2H), 1.19-1.13 (m, 2H), 0.80 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR: δ 151.1, 144.9, 132.8, 139.4, 137.6, 126.5, 117.5, 115.9, 115.4, 66.8, 50.9, 49.1, 47.4, 29.9, 19.7, 13.6 ppm. HRMS (ESI) *m/z* calculated for $C_{22}H_{28}O_3N_3S$ [(M + H)$^+$]: 414.1846, found 414.1857.



***N*-Cyclobutyl-3,4-dimethoxy-*N*-(4-morpholinobenzyl)benzenesulfonamide (13)** – Yield: 81 mg, 70%. ^{1}H NMR: δ 7.39 (d, *J* = 8.4 Hz, 1H), 7.28-7.20 (m, 3H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 8.4, 2H), 4.32 (s, 2H), 4.24-4.18 (m, 1H), 3.93 (s, 3H), 3.88 (s, 3H), 3.86 (m, 4H), 3.15 (m, 4H), 2.02-1.89 (m, 4H), 2.05-1.90 (m, 4H), 1.55-1.25 (m, 2H) ppm. ^{13}C NMR: δ 152.3, 150.5, 149.0 132.2, 129.8, 128.2, 120.9, 115.6, 110.6, 109.7, 66.9, 56.2, 56.1, 52.9, 49.4, 48.0, 29.7, 29.3, 15.1 ppm. HRMS (ESI) *m/z* calculated for $C_{23}H_{31}O_5N_2S$ [(M + H)$^{+}$]: 446.1948, found 447.1949.

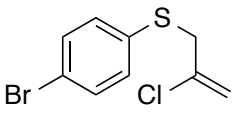


***N*-((2,2-Dimethyl-2*H*-chromen-6-yl)methyl)-3,4-dimethoxy-*N*-(2-morpholinoethyl)benzenesulfonamide (14)** – Yield: 31 mg, 49%. ^{1}H NMR: δ 7.45 (d, *J* = 8.4 Hz, 1H), 6.93 (t, *J* = 9.6 Hz, 2H), 6.85 (s, 1H), 6.67 (d, *J* = 8.4 Hz, 1H), 6.22 (d, *J* = 10.0 Hz, 1H), 5.58 (d, *J* = 10.0 Hz, 1H), 4.23 (s, 2H), 3.93 (s, 3H), 3.89 (s, 3H), 3.59 (s, 4H), 3.19 (t, *J* = 7.2 Hz, 2H), 2.32 (t, *J* = 7.2 Hz, 2H), 2.26 (s, 4H), 1.96 (s, 6H) ppm. ^{13}C NMR: δ 152.7, 152.5, 149.1, 131.8, 131.3, 129.1, 128.3, 126.5, 122.0, 121.4, 121.9, 116.3, 110.6, 109.8, 66.8, 57.3, 56.3, 56.2, 53.6, 52.2, 44.4, 27.9 ppm. HRMS (ESI) *m/z* calculated for $C_{26}H_{35}O_6N_2S$ [(M + H)$^{+}$]: 503.2210, found 503.2204.



***N*-((2,2-Dimethyl-2*H*-chromen-6-yl)methyl)-3,4-dimethoxy-*N*-(3-morpholinopropyl)benzenesulfonamide (15)** – Yield: 16 mg, 14%. ^{1}H NMR: δ 7.43 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 6.98-6.93 (m, 2H), 6.87 (s, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 6.23 (d, *J* = 10.0 Hz, 1H), 5.60 (d, *J* = 10 Hz, 1H), 4.19 (s, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 3.60 (s, 4H), 3.12 (t, *J* = 7.6 Hz, 2H), 2.22 (s, 4H), 2.18 (t, *J* = 8.0 Hz, 2H), 1.59-1.52 (m, 2H), 1.40 (s, 6H) ppm. ^{13}C NMR: δ 152.8, 152.4, 149.1, 131.6, 131.3, 129.3, 128.4, 126.5, 121.9, 121.3, 121.0, 116.3, 110.6, 109.8, 66.9, 56.3, 55.9, 53.4, 52.0, 46.2, 28.0, 25.4 ppm. HRMS (ESI) *m/z* calculated for $C_{27}H_{37}O_6N_2S$ [$(M + H)^+$]: 517.2367, found 517.2366.

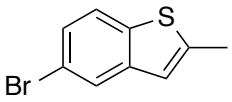
II. Hydroxymethine analogues



(4-bromophenyl)(2-chloroallyl)sulfane (16)

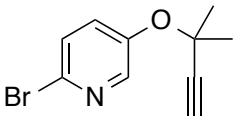
In a 50 mL three-neck round bottom flask, 100 mg (1 eq.) of 4-bromothiophenol, 146 mg of K_2CO_3 (2 eq.), 150 mg (1.7 eq) of KI and 5 mg (0.05 eq) of CuI were mixed in acetone (10 mL) and was put under argon gas. The solution was then heated up to 55^{o}C for 15 min and 106 mg (1.8 eq) of 2,3-dichloroprop-1-ene was added. The reaction mixture stirred for 6 h and was allowed to cool down to room temperature. The mixture was treated with DI H_2O (20 mL) and diethyl ether (20 mL). The ethereal layer was washed with brine (20 mL), dried over Na_2SO_4, and concentrated in vacuo.

The product was purified using flash column chromatography. Hexanes were used as eluent. Yield: 46 mg, 33%. ^{1}H NMR: δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 5.27 (s, 2H), 3.70 (s, 2H). ^{13}C NMR: δ 137.5, 133.8, 132.6, 132.1, 121.3, 115.1, 42.8 ppm.



5-bromo-2-methylbenzo[*b*]thiophene (17)

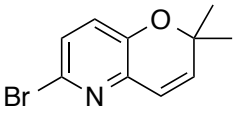
In a 50 mL round bottom flask, the sulfane product was treated with <1 mL of *N,N*-dimethylaniline and was stirred at 170^{o}C for 12 h. The solution was taken up in ethyl acetate (20 mL), washed with IM HCl (20 mL x 3), saturated $NaHCO_3$ solution (20 mL), brine 20 mL) and was dried over Na_2SO_4. The organic layer was concentrated in vacuo. The product was purified using flash column chromatography. Hexanes were used as eluent (1:8). Yield: 19 mg, 48%. ^{1}H NMR: δ 7.77 (d, *J* = 1.2 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.34 (dd, *J* = 8.8 Hz, 1.6 Hz, 1H), 6.90 (s, 1H), 2.59 (s, 3H) ppm. ^{13}C NMR: δ 132.2, 129.4, 126.3, 125.2, 123.3, 120.9, 16.2 ppm.



2-Bromo-5-((2-methylbut-3-yn-2-yl)oxy)pyridine (20a)

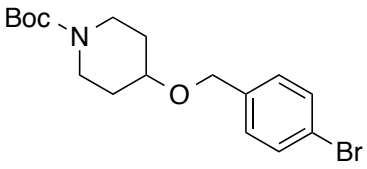
In a 100 mL round bottom flask, 2 g (0.012 mol) of 6-bromopyridin-3-ol was dissolved in dry acetonitrile (10 mL) and was cooled to 0^{o}C under Argon gas. To this solution, 9.0 mL (0.05 mol) of DBU was added and the solution was allowed to stir for 30 min. 6.8 mL (0.05 mol) of 3-chloro-3-methylbut-1-yne was then added into the mixture drop wise. The solution was allowed to warm up to room temperature and was stirred overnight. The solution was concentrated and was taken up with ethyl acetate (100 mL). The organic solution was washed with 1M HCl solution (20 mL),

1M NaOH solution (20 mL), saturated $NaHCO_3$ solution (20 mL), brine (20 mL) and was dried over Na_2SO_4. The organic layer was concentrated in vacuo and was taken directly to the next step.



6-Bromo-2,2-dimethyl-2*H*-pyrano[3,2-*b*]pyridine (20)

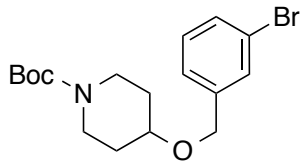
Using the impure product from the procedure above, the crude mixture was dissolved in *N,N*-dimethylaniline (<1 mL) at 170^{o}C for 6 h. The solution was taken up in ethyl acetate (20 mL), washed with IM HCl (20 mL x 3), saturated $NaHCO_3$ solution (20 mL), brine 20 mL) and was dried over Na_2SO_4. The organic layer was concentrated in vacuo. The product was purified using flash column chromatography. Hexanes were used as eluent. Yield: 239.4 mg, 34%. ^{1}H NMR: δ 7.10 (d, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.40 (d, *J* = 10.0 Hz, 1H), 5.83 (d, *J* = 10.0 Hz, 1H), 1.41 (s, 6H) ppm. ^{13}C NMR: δ 149.1, 142.1, 136.0, 131.3, 127.4, 125.9, 123.0, 28.2 ppm.



***Tert*-butyl 4-((4-bromobenzyl)oxy)piperidine-1-carboxylate (21)**

In a 100 mL round bottom flask, 2 g (0.012 mol) of tert-butyl 4-hydroxypiperidine-1-carboxylate and 295 mg (0.8 mmol) of TBAI was dissolved in dry THF (10 mL) and was cooled to 0^{o}C under inert atmosphere with Argon gas. To this solution, 480 mg (0.02 mol) of NaH was added and the solution was allowed to stir for 30 min. 2.4 g (0.008 mol) of 4-bromobenzyl bromide was then added into the mixture. The solution was allowed to warm up to room temperature and was stirred overnight. The solution

was quenched with saturated NH_4Cl solution (20 mL) and the organic layer was extracted up with ethyl acetate (50 mL), washed with brine (20 mL) and was dried over Na_2SO_4. The organic layer was concentrated in vacuo and was purified using flash column chromatography. Hexanes were used as eluent. Yield: 2 g, 64%. ^{1}H NMR: δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 4.48 (s, 2H), 3.77-3.74 (m, 2H), 3.55-3.51 (m, 1H), 3.12-3.06 (m, 2H), 1.82 (bs, 2H), 1.60-1.57 (m, 2H), 1.44 (s, 9H) ppm. ^{13}C NMR: δ 154.8, 137.9, 131.5, 129.1, 121.3, 79.5, 74.2, 69.1, 60.4, 41.0, 34.7, 31.6, 31.0, 28.4, 25.3, 22.7, 21.0, 14.2, 14.1 ppm.



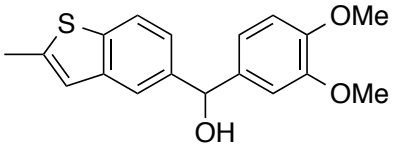
***Tert*-butyl 4-((3-bromobenzyl)oxy)piperidine-1-carboxylate (22)**

In a 50 mL round bottom flask, 120 mg (0.60 mmol) of tert-butyl 4-hydroxypiperidine-1-carboxylate and 15 mg (0.04 mmol) of TBAI was dissolved in dry THF (10 mL) and was cooled to 0^{o}C under inert atmosphere with Argon gas. To this solution, 24 mg (1.0 mmol) of NaH was added and the solution was allowed to stir for 30 min. 100 mg (0.40 mmol) of 4-bromobenzyl bromide was then added into the mixture. The solution was allowed to warm up to room temperature and was stirred overnight. The solution was quenched with saturated NH_4Cl solution (20 mL) and the organic layer was extracted up with ethyl acetate (20 mL), washed with brine (20 mL) and was dried over Na_2SO_4. The organic layer was concentrated in vacuo and was purified using flash column chromatography. Hexanes were used as eluent. Yield: 167 mg, 75%. ^{1}H NMR: δ 7.51(s, 1H), 7.42 (d, *J* = 6.4 Hz, 1H), 7.28-7.20 (m, 2H), 4.53-4.52 (s, 2H), 3.79-3.78 (m, 2H), 3.57-3.55 (m, 1H), 3.14-3.10 (m, 2H), 1.86 (bs, 2H), 1.61-

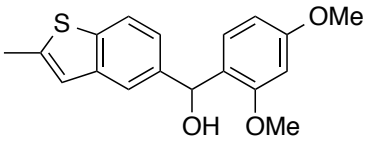
1.59 (m, 2H), 1.28 (s, 9H) ppm. ^{13}C NMR: δ 154.8, 141.1, 130.6, 130.3, 130.0, 125.8 122.6, 79.5, 74.4, 69.0, 31.0, 28.4 ppm.

General procedure for the synthesis of hydroxymethine products:

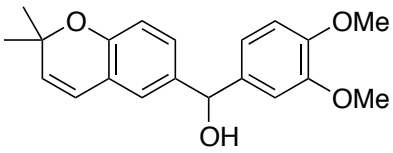
A flask of the aryl bromide (1 eq.) was degassed and anhydrous THF (10 mL) was added under nitrogen gas. The solution was cooled to -78^{o}C and stirred for 1 h. n-BuLi (0.9 eq) was then added to the solution drop wise. To this solution, the aldehyde (1.1 eq) was added dropwise and the reaction mixture was stirred for 1 h and was allowed to warm up to room temperature. The mixture was then quenched with saturated ammonium chloride solution (20 mL) and the organic layer was extracted with ethyl acetate (20 mL x 2), washed with brine (25 mL x 1), dried over Na_2SO_4 and concentrated in vacuo. The product was purified using flash column chromatography. Ethyl acetate and hexanes were used as eluent (1:3).



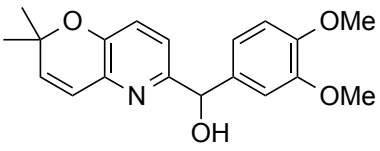
(3,4-Dimethoxyphenyl)(2-methylbenzo[*b*]thiophen-5-yl)methanol (18) – Yield: 3 mg, 12%. ^{1}H NMR: δ 7.70 (s, 1H), 7.67 (d, *J* = 4.0 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 6.94 (s, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 5.90 (s, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 2.58 (s, 3H) ppm, 2.20 (d, *J* = 2 Hz, 1H). HRMS (ESI) *m/z* calculated for $C_{18}H_{18}O_3S + Na^+$: 337.0874, found 337.0883.



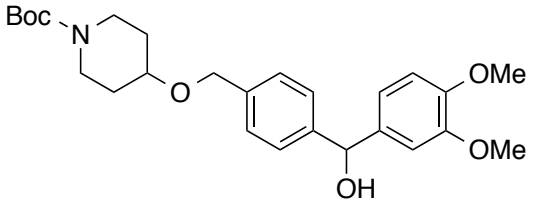
(2,4-Dimethoxyphenyl)(2-methylbenzo[*b*]thiophen-5-yl)methanol (19) – Yield: 3 mg, 14%. ^{1}H NMR: δ 7.67 (d, *J* = 4.8 Hz, 2H), 7.24 (s, 1H), 7.07 (d, *J* = 4.0 Hz, 1H), 6.94 (s, 1H), 6.47 (s, 1H), 6.44 (d, *J* = 8.4 Hz, 1H), 6.10 (d, *J* = 4.8 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 2.92 (d, *J* = 5.2 Hz, 1H), 2.57 (s, 3H) ppm. HRMS (ESI) *m/z* calculated for $C_{18}H_{18}O_3S + Na^+$: 337.0874, found 337.0863.



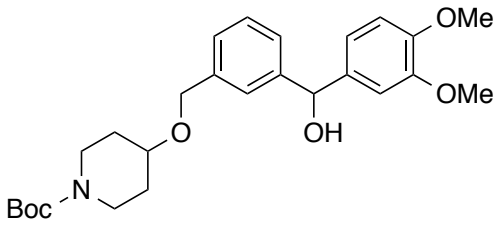
(3,4-Dimethoxyphenyl)(2,2-dimethyl-2*H*-chromen-6-yl)methanol (24) - Yield: 104 mg, 63%. ^{1}H NMR: δ 7.09 (d, *J* = 8.0 Hz, 1H), 6.98 (s, 1H), 6.94 (s, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.29 (d, J = 9.6 Hz, 1H), 5.72 (s, 1H), 5.61 (d, *J* = 9.6 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 2.20 (s, 1H), 1.43 (s, 6H) ppm. ^{13}C NMR: δ 152.4, 149.0 148.4, 136.7, 136.3, 130.9, 127.4, 124.6, 122.3, 121.1, 118.8, 116.2, 110.9, 109.7, 76.3, 75.5, 55.9, 55.9, 28.0, 28.0 ppm. HRMS (ESI) *m/z* calculated for $C_{20}H_{22}O_4 + Na^+$: 349.1416, found 349.1419.



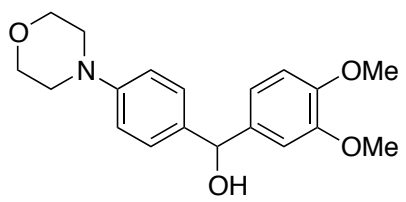
(3,4-Dimethoxyphenyl)(2,2-dimethyl-2*H*-pyrano[3,2-*b*]pyridin-6-yl)methanol (25) – Yield: 69 mg, 53%. ^{1}H NMR: δ 6.95 (d, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 5.2 Hz, 2H), 6.80 (d, *J* = 4.4 Hz, 2H), 6.79 (dd, *J* = 8.4, 4 Hz, 2H), 6.50, (d, *J* = 10.0 Hz, 1H) 5.85 (d, *J* = 10.0 Hz, 1H), 5.58 (s, 1H), 5.14 (bs, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 1.43 (s, 6H) ppm. ^{13}C NMR: 152.8, 149.1, 148.7, 148.6, 139.2, 136.1, 135.3, 124.0, 123.6, 121.1, 119.5, 119.3, 111.0,110.4, 74.4, 55.9, 55.8, 28.3 ppm.



***Tert*-butyl 4-((4-((3,4-dimethoxyphenyl)(hydroxy)methyl)benzyl)oxy)piperidine-1-carboxylate (26)** - Yield: 877 mg, 54%. ^{1}H NMR: δ 7.35 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 1.6 Hz, 1H), 6.88-6.86 (m, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 5.78 (s, 1H), 4.52 (s, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.77-3.73 (m, 2H), 3.57-3.51 (m, 1H), 3.11-3.05 (m, 2H), 2.39(s, 1H), 1.84-1.82(m, 2H), 1.58-1.55(m, 2H), 1.44 (s, 9H) ppm. ^{13}C NMR: δ 149.1, 143.3, 137.9, 136.6, 127.6, 126.5, 118.9, 110.9, 109.7, 79.5, 75.8, 74.0, 69.6, 60.4, 55.9, 55.8, 28.4, 21.0, 14.2 ppm.



***Tert*-butyl 4-((3-((3,4-dimethoxyphenyl)(hydroxy)methyl)benzyl)oxy)piperidine-1-carboxylate (27)** – Yield: 41 mg, 33%. ^{1}H NMR: δ 7.74 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.2 Hz, 1H), 7.50-7.34 (m, 2H), 7.38 (d, *J* = 8.4 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 5.80 (s, 1H), 4.62 (s, 2H), 3.97 (s, 3H), 3.95 (s, 3H), 3.76 (bs, 2H), 3.60 (m, 1H), 3.14-3.08 (m, 2H), 2.46 (s,1H), 1.85 (bs, 2H), 1.62 (bs, 2H), 1.48 (s, 9H) ppm. ^{13}C NMR: δ 154.8, 149.0 148.4, 144.3, 138.8, 136.7, 128.5, 126.5, 125.7, 125.5, 119.0, 110.9, 109.9, 79.5, 75.7, 74.1, 69.8, 55.9, 55.8, 41.2, 34.1, 31.0, 28.4 ppm.

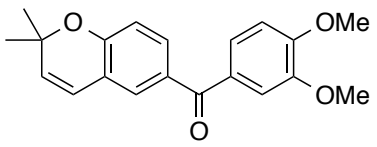


(3,4-Dimethoxyphenyl)(4-morpholinophenyl)methanol (28) - Yield: 167 mg, 55%. ^{1}H NMR: δ 7.25 (d, *J* = 8.0 Hz, 2H), 6.92 (s, 1H), 6.87-6.80 (m, 4H), 5.70 (s, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.82 (m, 4H), 3.12-3.10 (m, 4H), 2.80 (bs, 1H) ppm. ^{13}C NMR: δ 150.6, 148.9, 148.2, 136.9, 135.7, 127.5, 118.8, 115.6, 110.8, 109.7, 75.4, 66.8, 66.5, 55.9, 55.87, 49.3 ppm. HRMS (ESI) *m/z* calculated for $C_{19}H_{24}NO_4$ [(M + H)$^{+}$] 330.1705, found 330.1710.

III. Ketone derivatives from hydroxymethine products

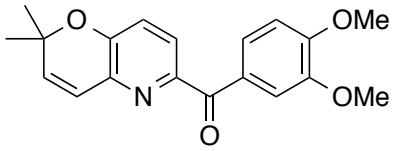
General procedure for the ketone products:

To a solution of 50 mg of hydroxymethine product (1 eq.) in DCM (10 mL) was added Celite (33 mg Celite/ hydroxymethine product) as solid support. The reaction mixture was then charged with the appropriate amounts of PCC (2 eq) and was allowed to stir at room temperature for 24 h. The solution mixture was filtered and washed with DCM (20 mL x 3) and concentrated in vacuo. The crude product was purified using flash column chromatography. Ethyl acetate and hexanes were used as eluent (1:10).

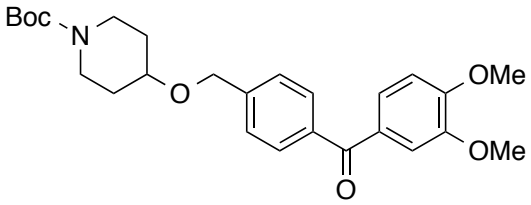


(3,4-Dimethoxyphenyl)(2,2-dimethyl-2*H*-chromen-6-yl)methanone (29) – Yield: 77 mg, 74%. ^{1}H NMR: δ 7.49 (d, *J* = 8.4 Hz, 1H), 7.41 (s, 1H), 7.34 (s, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.26 (d, *J* = 10.0 Hz, 1H), 5.58 (d, *J* = 10.0 Hz, 1H), 3.87(s, 3H), 3.85 (s, 3H), 1.39 (s, 6H) ppm. ^{13}C NMR:

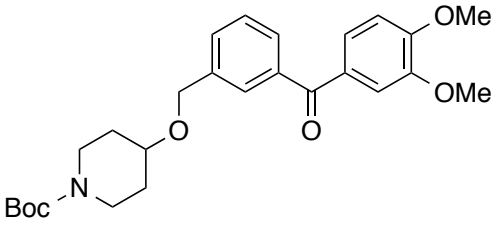
δ 194.3, 171.1, 156.7, 152.5, 149.0, 131.9, 131.2, 130.8, 130.7, 128.6, 124.7, 121.7, 120.6, 115.8, 112.2, 109.7, 60.3, 56.1, 56.0, 28.4, 21.0, 14.2 ppm. HRMS (ESI) *m/z* calculated for $C_{20}H_{21}O_4$ [(M + H)$^+$]: 325.1440, found 325.1433.



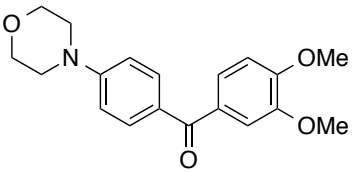
(3,4-Dimethoxyphenyl)(2,2-dimethyl-2*H*-pyrano[3,2-*b*]pyridin-6-yl)methanone (30) – Yield: 44 mg, 64%. ^{1}H NMR: δ 7.87-7.83 (m, 2H), 7.79 (s, 1H), 7.15 (d *J* = 8.4 Hz,1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.56 (d, *J* = 10.0 Hz, 1H), 5.976 (d, *J* = 10.0 Hz, 1H), 3.96 (s,3H), 3.95 (s, 3H), 1.53 (s, 6H) ppm. ^{13}C NMR: δ 190.9, 153.0, 152.0, 148.6, 147.7, 139.6, 135.7, 130.0, 126.6, 126.1, 123.8, 123.1, 113.3, 109.8, 78.2, 56.1, 56.0, 28.7 ppm. HRMS (ESI) *m/z* calculated for $C_{19}H_{20}O_4N$ [(M + H)$^+$]: 326.1387, found 326.1392.



***Tert*-butyl 4-((4-(3,4-dimethoxybenzoyl)benzyl)oxy)piperidine-1-carboxylate (31)** – Yield: 594 mg, 68% ^{1}H NMR: δ 7.69 (d, *J* = 8.4 Hz, 2H), 7.42-7.39 (m, 3H), 7.31 (d, *J* = 8.4 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 4.58 (s, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.75-3.72, (m, 2H), 3.56-3.54 (m, 1H), 3.10-3.04 (m, 2H), 1.96 (s, 1H), 1.82 (bs, 2H), 1.59-1.53 (m, 2H), 1.40 (s, 9H) ppm. ^{13}C NMR: δ 195.1, 171.0, 154.8, 153.0, 148.9, 143.0, 137.4, 130.2, 130.0, 126.9, 125.4, 112.1, 109.8, 79.4, 74.5, 69.3, 60.3, 56.0, 55.9, 41.1, 31.0, 28.4, 21.0, 14.2 ppm. HRMS (ESI) *m/z* calculated for $C_{26}H_{33}O_6N$ + Na^+: 478.2200, found 478.2199.

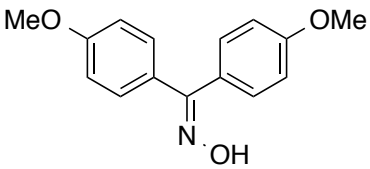


***Tert*-butyl 4-((3-(3,4-dimethoxybenzoyl)benzyl)oxy)piperidine-1-carboxylate (32)** – Yield: 16 mg, 54%. ^{1}H NMR: δ 7.73 (s, 1H), 7.75 (d, *J* = 7.2 Hz, 1H), 7.56 (d, *J* = 7.2 Hz, 1H), 7.49 (s, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.37 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.88 (d, *J* = 8.4, 1H), 4.61 (s, 2H), 3.96 (s, 3H), 3.94 (s, 3H), 3.76 (m, 2H), 3.61-3.57 (m, 1H), 3.13-3.07 (m, 3H), 1.86 (bs, 2H), 1.66-1.58 (m, 2H), 1.45 (s, 9H) ppm. ^{13}C NMR: δ 195.5, 154.5, 153.1, 149.0, 139.1, 138.4, 130.9, 130.2, 129.0, 128.6, 128.2, 125.5, 112.1, 109.8, 79.5, 74.5, 69.5, 56.1, 56.0, 31.0, 28.4 ppm. HRMS (ESI) *m/z* calculated for $C_{26}H_{33}O_6N + Na^+$: 478.2200, found 478.2197.



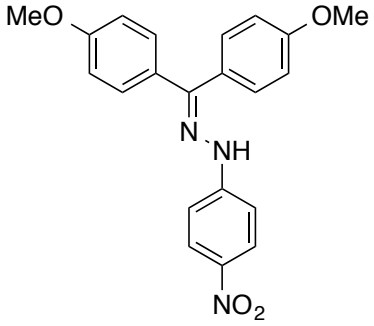
(3,4-Dimethoxyphenyl)(4-morpholinophenyl)methanone (33) – Yield: 45 mg, 42%. ^{1}H NMR: δ 7.76 (d, *J* = 8.8 Hz, 2H), 7.39 (s, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 6.89-6.87 (m, 3H), 3.93 (s, 3H), 3.91 (s, 3H), 3.84-3.82 (m, 4H), 3.30-3.27 (m, 4H) ppm. ^{13}C NMR: δ 194.1, 153.8, 152.3, 148.8, 132.2, 131.2, 128.4, 124.5, 113.3, 112.3, 109.8, 66.6, 56.1, 56.0, 47.7 ppm. HRMS (ESI) *m/z* calculated for $C_{19}H_{22}O_4N$ [$(M + H)^+$]: 328.1543, found 328.1538.

IV. Miscellaneous compounds:



Procedure for the synthesis of oxime product (34)

To a solution of 133 mg of bis(4-methoxyphenyl)methanone (1 eq.) in MeOH (10 mL) was added 0.22 mL of pyridine (5 eq.) The solution was then charged with 153 mg of hydroxylamine hydrochloride (4 eq.) and was allowed to stir at room temperature for 36 h. The mixture was concentrated and the solid obtained was dissolved in DCM (20 mL). The solution was washed with 1M HCl solution (20 mL), saturated $NaHCO_3$ solution (20 mL), brine (20 mL), dried over Na_2SO_4 and concentrated in vacuo. The product was purified using flash column chromatography. Ethyl acetate and hexanes were used as eluent (1:6). Yield: 79 mg, 56%. ^{1}H NMR: δ 7.44-7.40 (m, 4H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 3.86 (s, 3H), 3.82 (s, 3H) ppm. ^{13}C NMR: δ 160.7, 160.0, 157.0, 131.2, 129.5, 129.3, 125.0, 113.8, 113.6, 55.4, 55.3 ppm. HRMS (ESI) *m/z* calculated for $C_{15}H_{16}NO_3$ [$(M + H)^+$]: 258.1130, found 258.1123.



Procedure for the synthesis of the hydrazone product (35):

In a heavy-walled glass vial sealed with a Teflon septum, 40 mg of bis(4-methoxyphenyl)methanone (1 eq) was dissolved in MeOH (5 mL) was mixed with 160 mg of (4-nitrophenyl)hydrazine (4 eq.) and 0.66 mL of pyridine (5 eq.). The solution was irradiated with microwave for 5 min at 150 ^{o}C at 35W. The mixture was concentrated and the solid obtained was dissolved in DCM (20 mL). The solution was washed with 1M HCl solution (20 mL), saturated $NaHCO_3$ solution (20 mL), brine (20 mL), dried over Na_2SO_4 and concentrated in vacuo. The product was

purified using flash column chromatography. Ethyl acetate and hexanes were used as eluent (1:8). Yield: 63 mg, 79%. ^{1}H NMR: δ 8.15 (d, *J* = 9.2 Hz, 2H), 7.89 (s, 1H), 7.56 (d, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 3.91 (s, 3H), 3.85 (s, 3H) ppm. ^{13}C NMR: δ 160.6, 160.5, 149.6, 148.8, 139.9, 132.2, 130.5, 130.3, 128.6, 126.1, 123.8, 115.2, 115.2, 113.7, 113.5, 111.8, 55.4, 55.3 ppm. HRMS (ESI) *m/z* calculated for $C_{21}H_{20}O_4N_3$ [$(M + H)^+$]: 378.1448, found 378.1444.

APPENDIX

Section 1:

^{1}H NMR of compound **2** 53

^{13}C NMR of compound **2** 54

^{1}H NMR of compound **3** 55

^{13}C NMR of compound **3** 56

^{1}H NMR of compound **4** 57

^{13}C NMR of compound **4** 58

^{1}H NMR of compound **5** 59

^{13}C NMR of compound **5** 60

^{1}H NMR of compound **6** 61

^{13}C NMR of compound **6** 62

^{1}H NMR of compound **7** 63

^{13}C NMR of compound **7** 64

^{1}H NMR of compound **8** 65

^{13}C NMR of compound **8** 66

^{1}H NMR of compound **9** 67

^{13}C NMR of compound **9** 68

^{1}H NMR of compound **10** 69

^{13}C NMR of compound **10** 70

^{1}H NMR of compound **11** 71

^{13}C NMR of compound **11** 72

^{1}H NMR of compound **12** 73

^{13}C NMR of compound **12** 74

^{1}H NMR of compound **13** 75

^{13}C NMR of compound **13** 76

^{1}H NMR of compound **14** 77

^{13}C NMR of compound **14** 78

^{1}H NMR of compound **15** 79

^{13}C NMR of compound **15** 80

^{1}H NMR of compound **16** 81

^{13}C NMR of compound **16** 82

^{1}H NMR of compound **17** 83

^{13}C NMR of compound **17** 84

^{1}H NMR of compound **18** 85

^{1}H NMR of compound **19** 86

^{1}H NMR of compound **20** 87

^{13}C NMR of compound **20** 88

^{1}H NMR of compound **21** 89

^{13}C NMR of compound **21** 90

^{1}H NMR of compound **22** 91

^{13}C NMR of compound **22** 92

^{1}H NMR of compound **24** 93

^{13}C NMR of compound **24** 94

^{1}H NMR of compound **25** 95

^{13}C NMR of compound **25** 96

^{1}H NMR of compound **26** 97

^{13}C NMR of compound **26** 98

^{1}H NMR of compound **27** 99

^{13}C NMR of compound **27** 100

^{1}H NMR of compound **28** 101

^{13}C NMR of compound **28** 102

^{1}H NMR of compound **29** 103

^{13}C NMR of compound **29** 104

^{1}H NMR of compound **30** 105

^{13}C NMR of compound **30** 106

^{1}H NMR of compound **31** 107

^{13}C NMR of compound **31** 108

^{1}H NMR of compound **32** 109

^{13}C NMR of compound **32** 110

^{1}H NMR of compound **33** 111

^{13}C NMR of compound **33** 112

^{1}H NMR of compound **34** 113

^{13}C NMR of compound **34** 114

^{13}C NMR of compound **35** 115

^{1}H NMR of compound **35** 116

Section II:

HRMS spectrum of compound **3** 117

HRMS spectrum of compound **4** 119

HRMS spectrum of compound **5** 120

HRMS spectrum of compound **6** 121

HRMS spectrum of compound **7** 122

HRMS spectrum of compound **8** 123

HRMS spectrum of compound **9** 125

HRMS spectrum of compound **10** 127

HRMS spectrum of compound **11** 129

HRMS spectrum of compound **12** 131

HRMS spectrum of compound **13** 133

HRMS spectrum of compound **14** 135

HRMS spectrum of compound **15** 137

HRMS spectrum of compound **18** 139

HRMS spectrum of compound **19** 141

HRMS spectrum of compound **29** 143

HRMS spectrum of compound **30** 145

HRMS spectrum of compound **31** 147

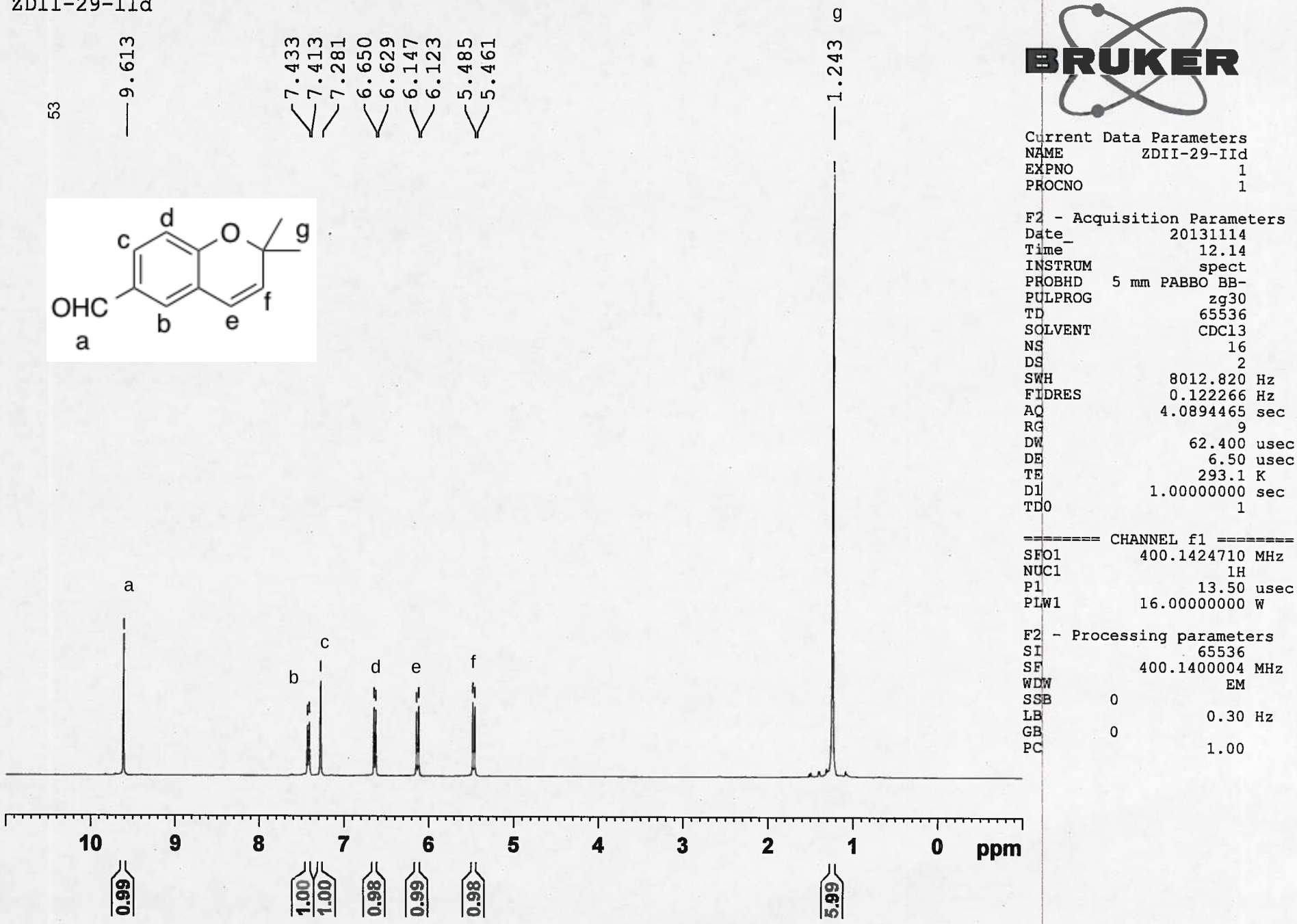
HRMS spectrum of compound **32** 149

HRMS spectrum of compound **33** 151

HRMS spectrum of compound **34** 153

HRMS spectrum of compound **35** 156

ZDII-29-IId



BRUKER

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PROCNO 1

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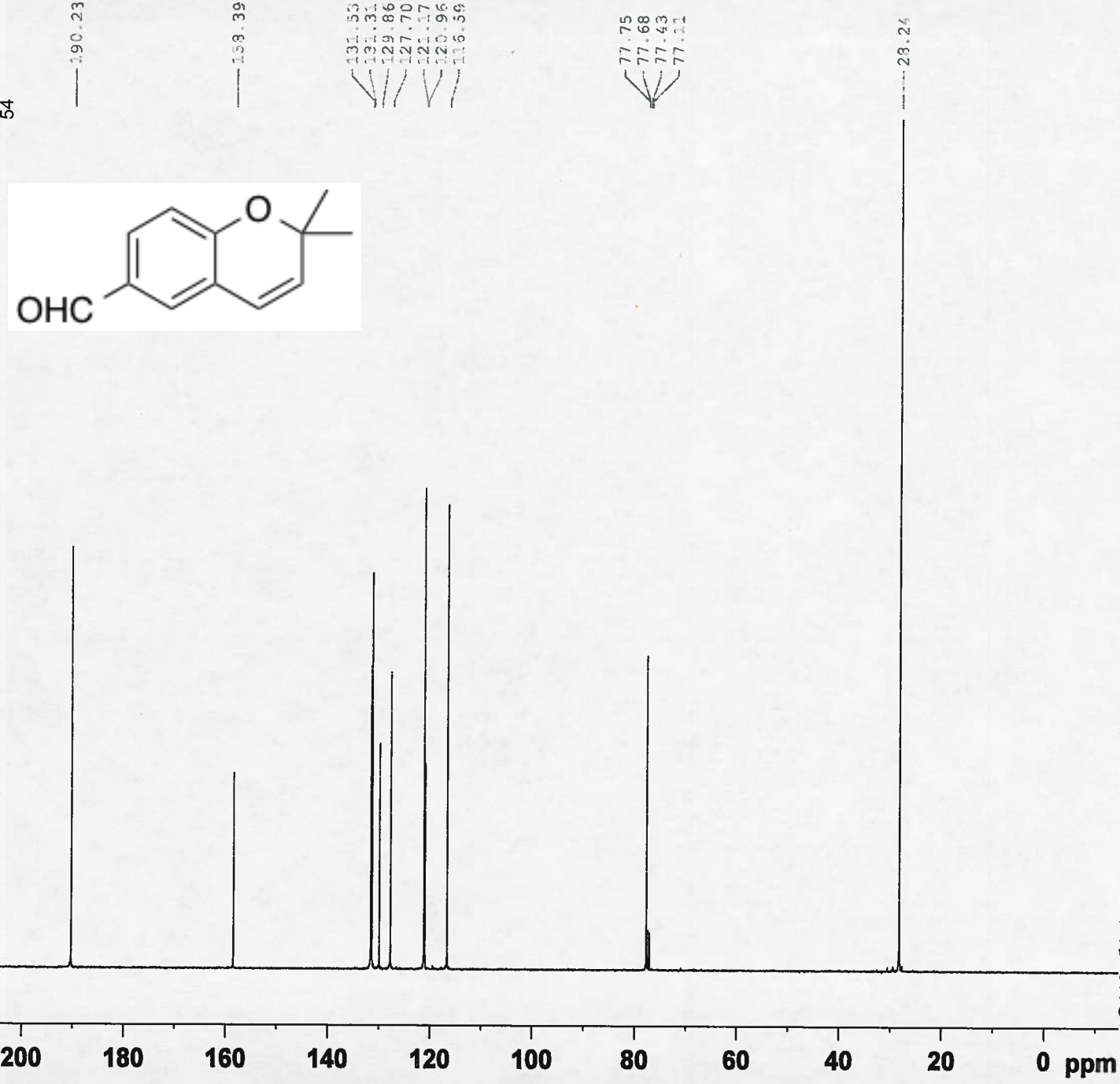
ZDII-29-IId-13C



BRUKER

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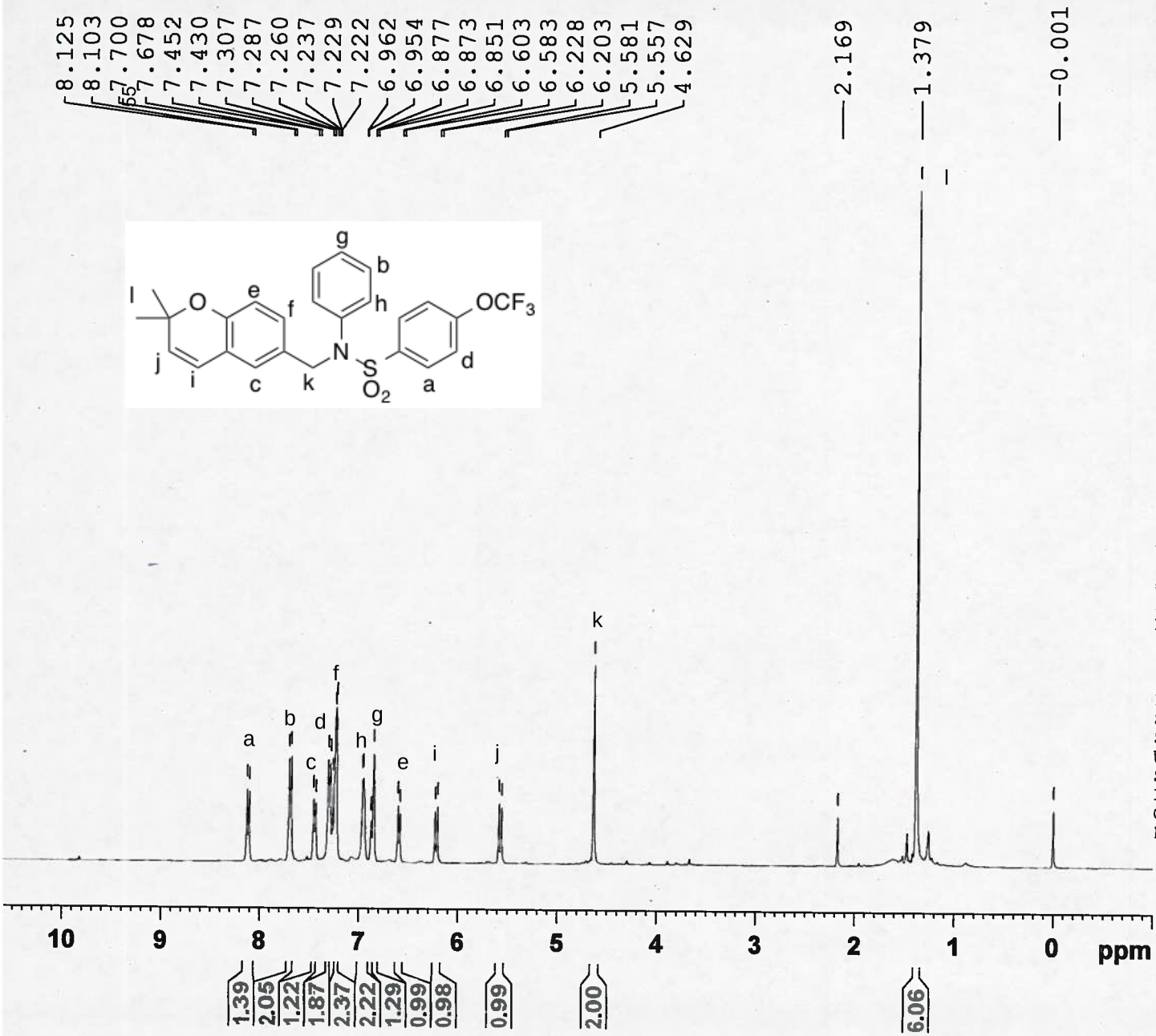
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

-I-33



Current Data Parameters

NAME	ZD-I-33
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20120719
Time	10.17
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	32
DW	62.400 usec
DE	6.50 usec
TE	297.8 K
D1	1.00000000 sec
TD0	1

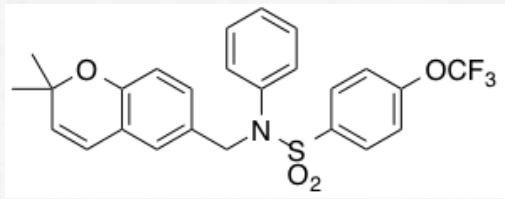
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400074 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZD-I-33




```
Current Data Parameters
NAME                  ZD-I-33
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_                20120719
Time                    10.20
INSTRUM                 spect
PROBHD    5 mm PABBO BB-
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                        128
DS                          4
SWH                 24038.461 Hz
FIDRES               0.366798 Hz
AQ                  1.3631488 sec
RG                        203
DW                     20.800 usec
DE                      6.50 usec
TE                     298.3 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
SFO1               100.6253441 MHz
NUC1                       13C
P1                      9.00 usec
PLW1               62.00000000 W

======== CHANNEL f2 ========
SFO2               400.1416006 MHz
NUC2                       1H
CPDPRG[2                waltz16
PCPD2                   90.00 usec
PLW2               16.00000000 W
PLW12               0.36000001 W
PLW13               0.29159999 W

F2 - Processing parameters
SI                         32768
SF                 100.6152830 MHz
WDW                           EM
SSB          0
LB                      1.00 Hz
GB           0
PC                      1.40
```

ZD1-34C

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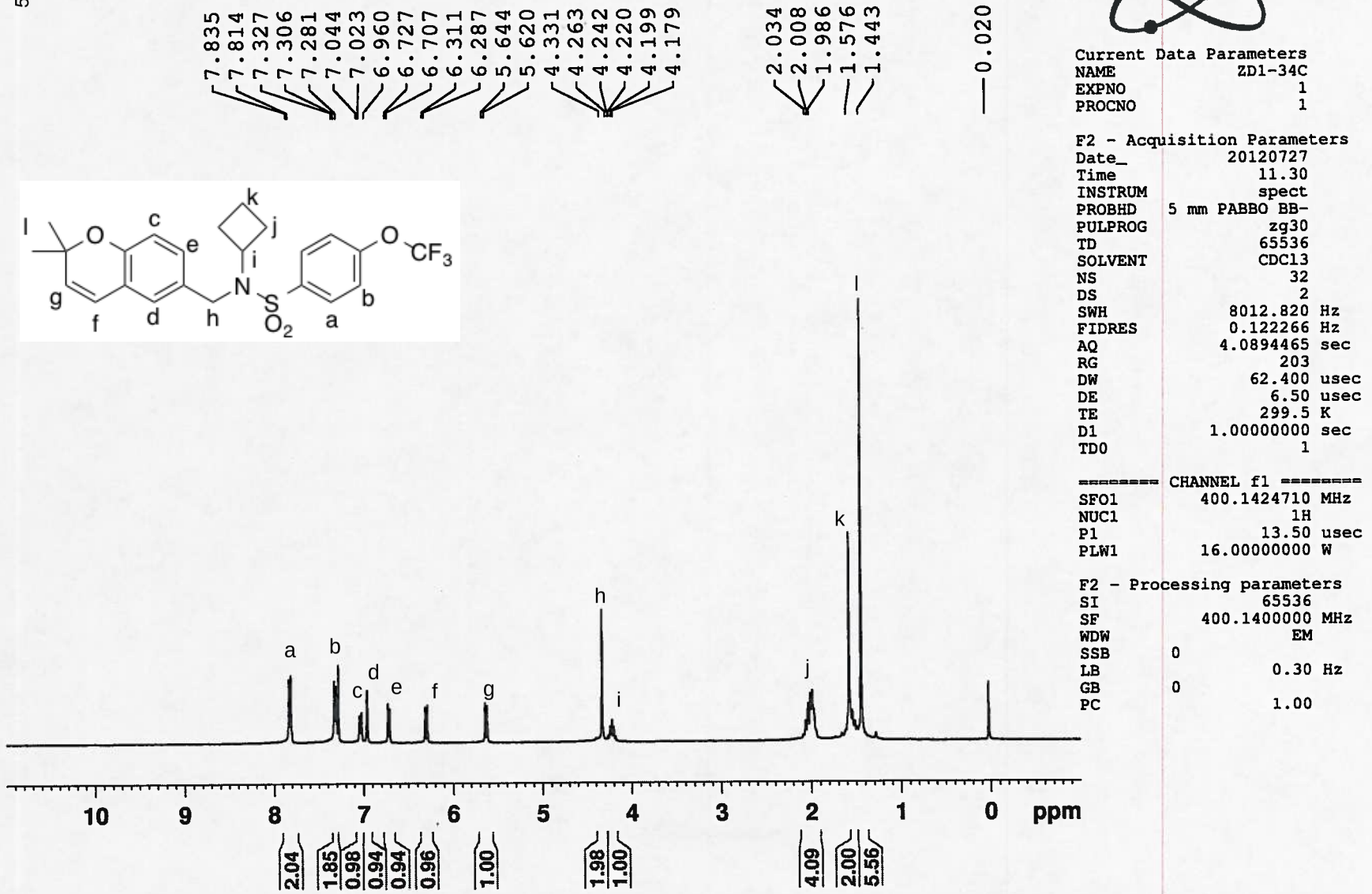


Current Data Parameters

NAME	ZD1-34C
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20120727
Time	11.30
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	32
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	203
DW	62.400 usec
DE	6.50 usec
TE	299.5 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========

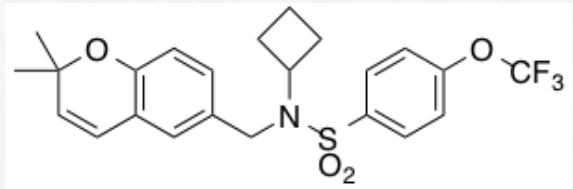
SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZD1-34C

58



Current Data Parameters

NAME	ZD1-34C
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20120727
Time	14.25
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	366
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	299.9 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	100.6253441 MHz
NUC1	13C
P1	9.00 usec
PLW1	62.00000000 W

======== CHANNEL f2 ========

SFO2	400.1416006 MHz
NUC2	1H
CPDPRG[2	waltz16
PCPD2	90.00 usec
PLW2	16.00000000 W
PLW12	0.36000001 W
PLW13	0.29159999 W

F2 - Processing parameters

SI	32768
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.20

ZD1-35C

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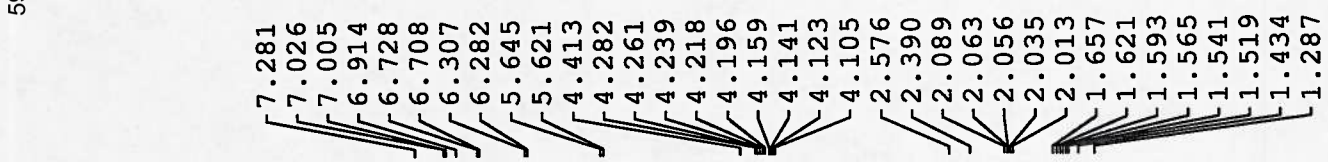

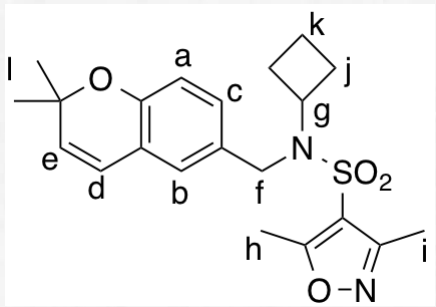

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Current Data Parameters

NAME	ZD1-35C
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20120727
Time	11.42
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	35
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	64
DW	62.400 usec
DE	6.50 usec
TE	299.4 K
D1	1.00000000 sec
TD0	1

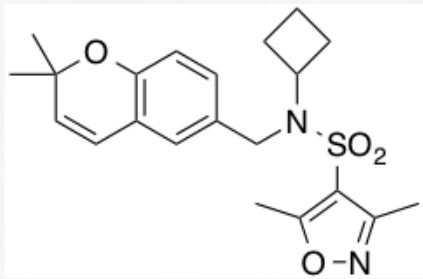
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

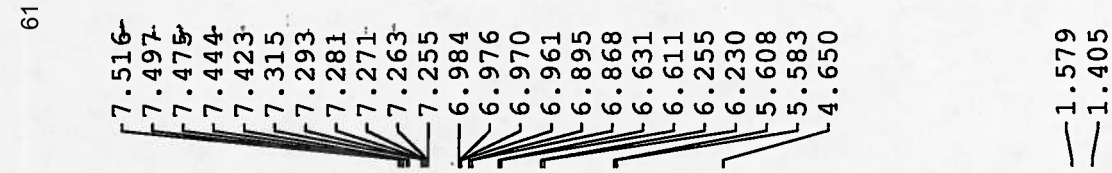
SI	65536
SF	400.1400000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

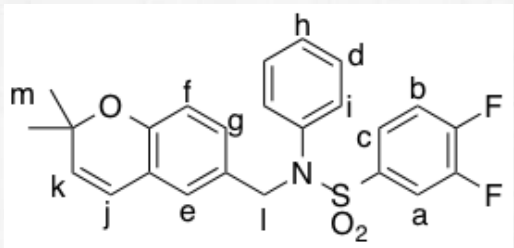
ZD1-35C




```
Current Data Parameters
NAME                  ZD1-35C
EXPNO                       2
PROCNO                      1

F2 - Acquisition Parameters
Date_              20120727
Time                  14.48
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      36
DS                       4
SWH             24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631488 sec
RG                     203
DW                  20.800 usec
DE                   6.50 usec
TE                  300.0 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
SFO1            100.6253441 MHz
NUC1                    13C
P1                    9.00 usec
PLW1            62.00000000 W

======== CHANNEL f2 ========
SFO2            400.1416006 MHz
NUC2                    1H
CPDPRG[2             waltz16
PCPD2                90.00 usec
PLW2            16.00000000 W
PLW12            0.36000001 W
PLW13            0.29159999 W

F2 - Processing parameters
SI                      32768
SF              100.6152830 MHz
WDW                     EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```

ZD-I-38





Current Data Parameters

NAME	ZD-I-38
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20120830
Time	13.36
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	128
DW	62.400 usec
DE	6.50 usec
TE	298.1 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========

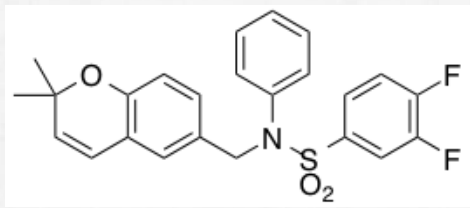
SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZD-I-38

62



Current Data Parameters

NAME	ZD-I-38
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20120830
Time	13.40
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	42
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	298.8 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	100.6253441 MHz
NUC1	13C
P1	9.00 usec
PLW1	62.00000000 W

======== CHANNEL f2 ========

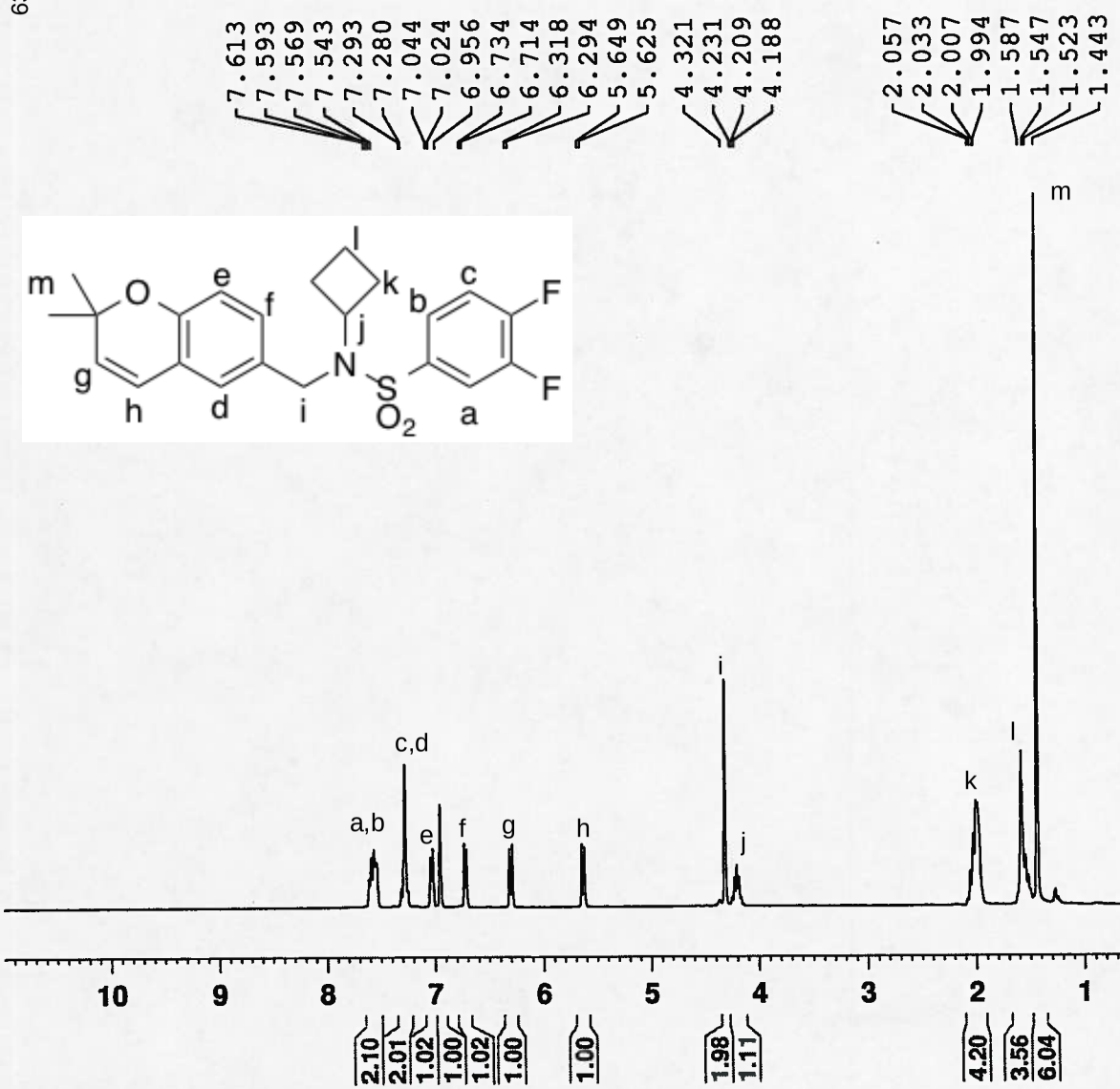
SFO2	400.1416006 MHz
NUC2	1H
CPDPRG[2	waltz16
PCPD2	90.00 usec
PLW2	16.00000000 W
PLW12	0.36000001 W
PLW13	0.29159999 W

F2 - Processing parameters

SI	32768
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

ZD-I-39

63



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Current Data Parameters

NAME	ZD-I-39
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20130118
Time	10.02
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	203
DW	62.400 usec
DE	6.50 usec
TE	294.0 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========

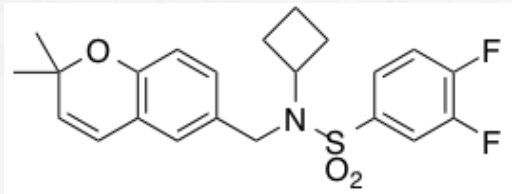
SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZD-I-39

64



Current Data Parameters

NAME	ZD-I-39
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20130118
Time	10.05
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	113
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	100.6253441 MHz
NUC1	13C
P1	9.00 usec
PLW1	62.00000000 W

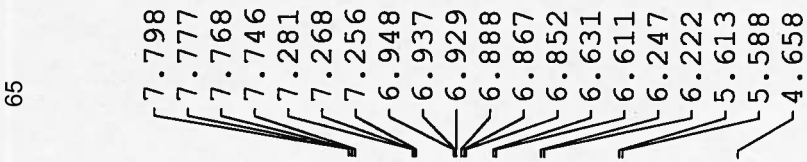
======== CHANNEL f2 ========

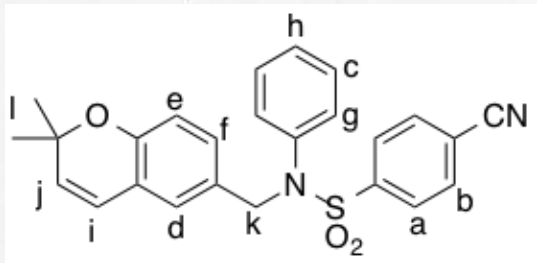
SFO2	400.1416006 MHz
NUC2	1H
CPDPRG[2	waltz16
PCPD2	90.00 usec
PLW2	16.00000000 W
PLW12	0.36000001 W
PLW13	0.29159999 W

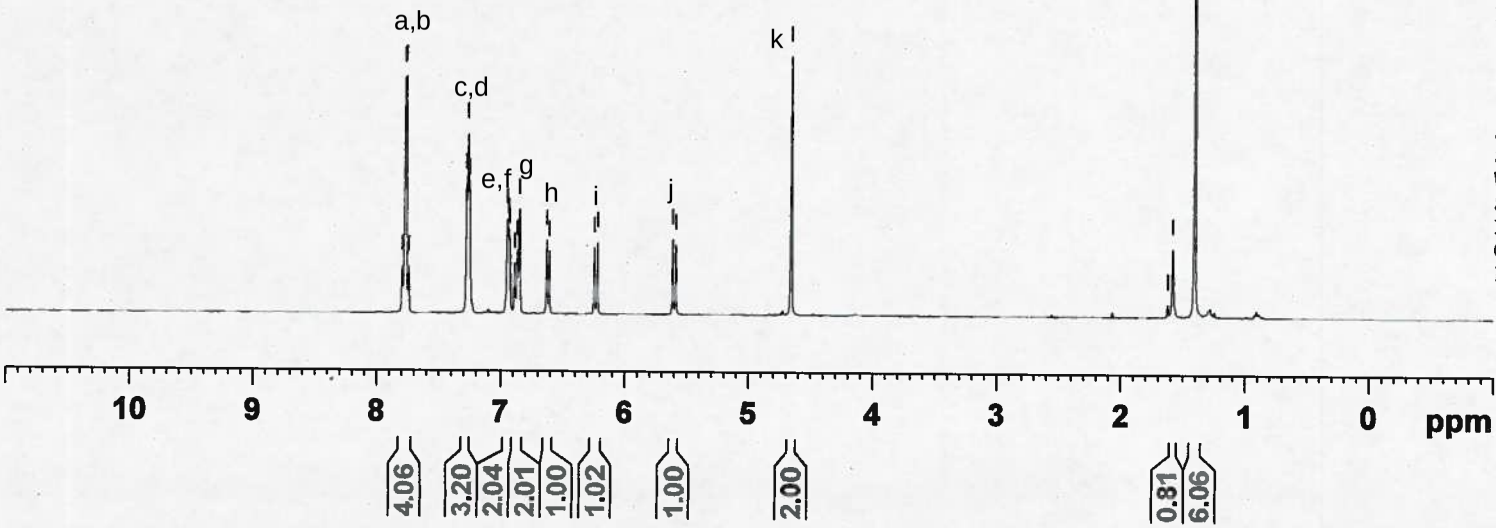
F2 - Processing parameters

SI	32768
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

ZDI-61c







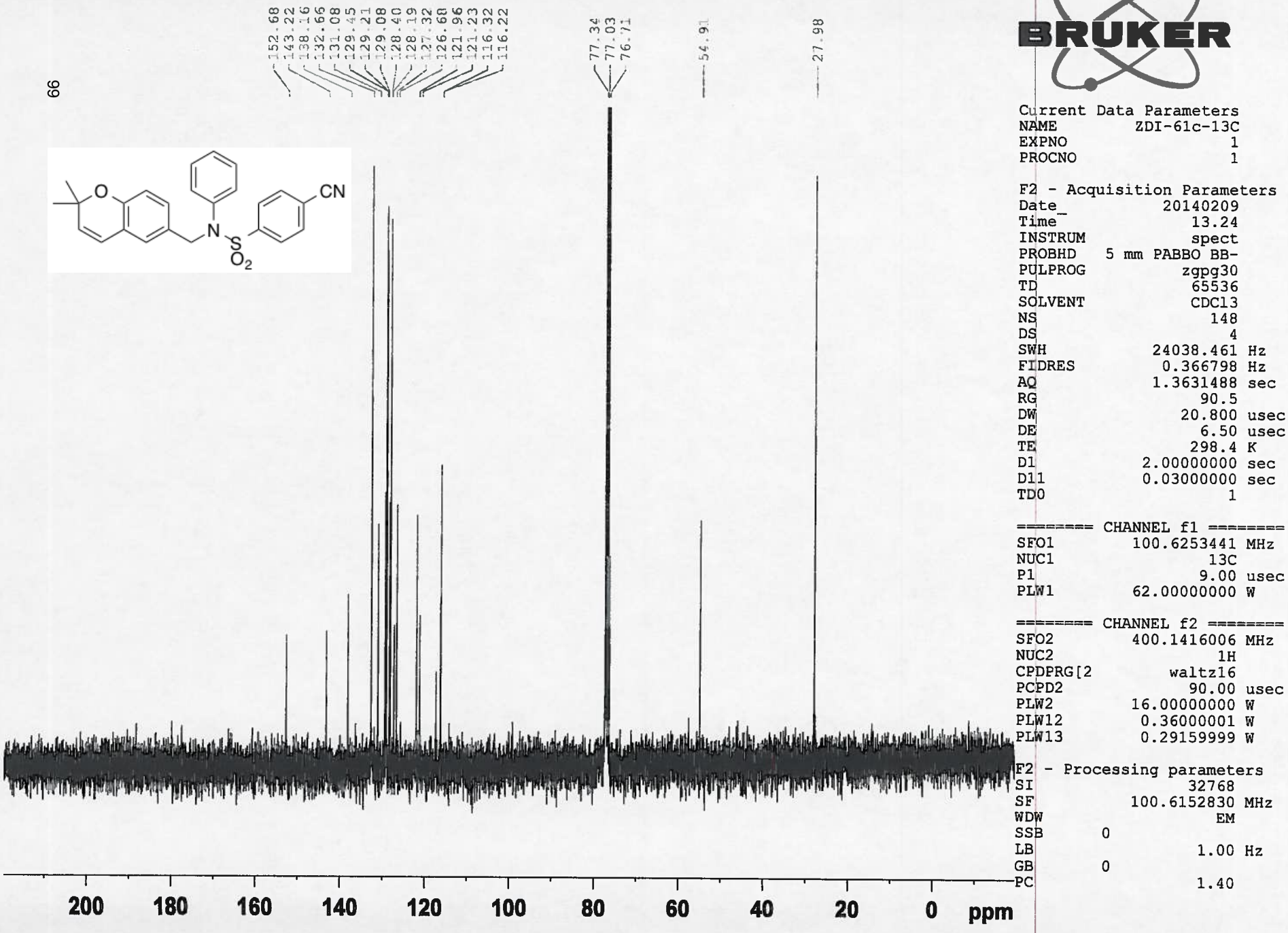
Current Data Parameters
NAME ZDI-61c
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140209
Time 13.23
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 1
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 161
DW 62.400 usec
DE 6.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

ZDI-61c-13C



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Current Data Parameters
NAME ZDI-61c-13C
EXPNO 1
PROCNO 1

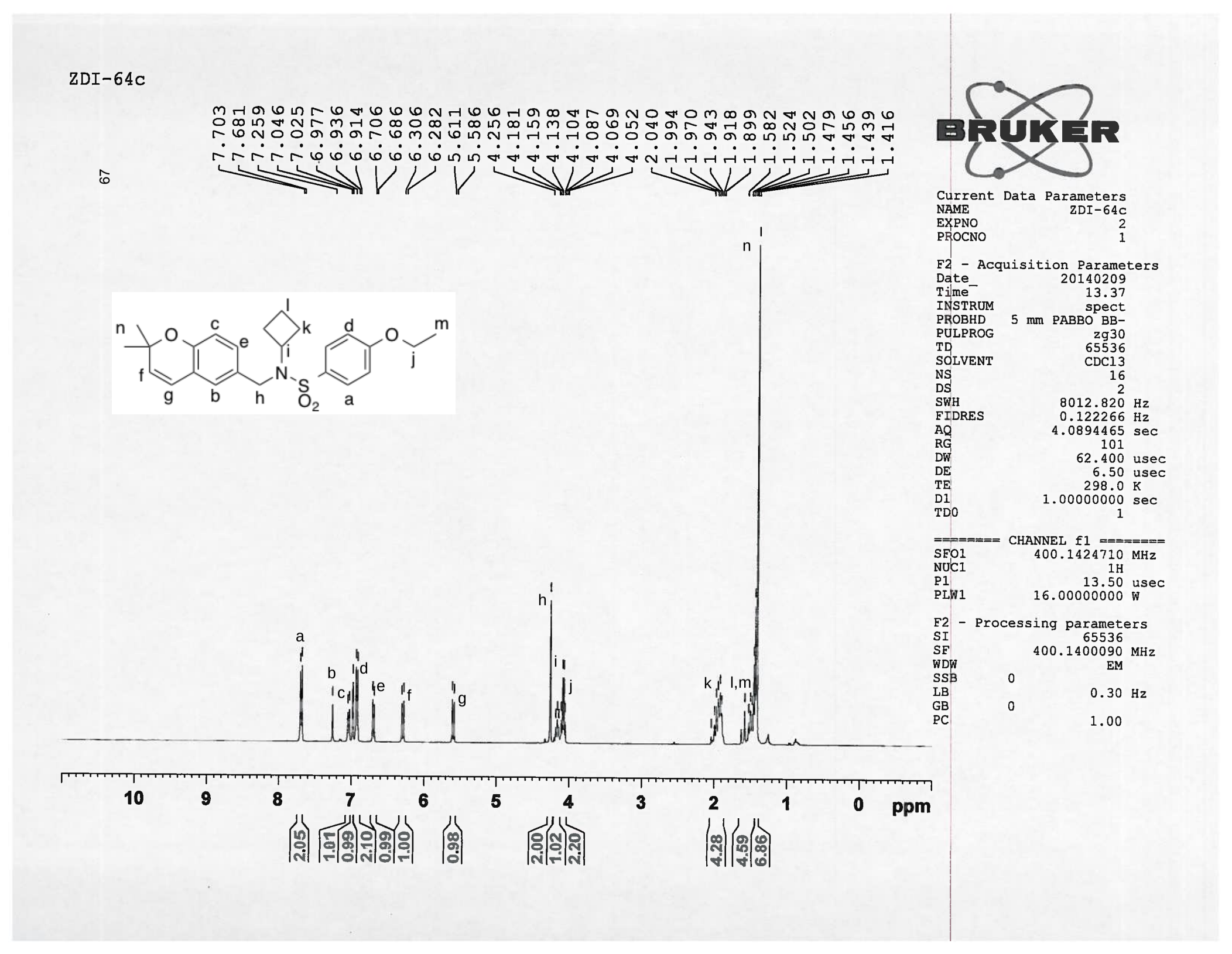
F2 - Acquisition Parameters
Date_ 20140209
Time 13.24
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 148
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 90.5
DW 20.800 usec
DE 6.50 usec
TE 298.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDI-64c



Current Data Parameters

NAME	ZDI-64c
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20140209
Time	13.37
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	101
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

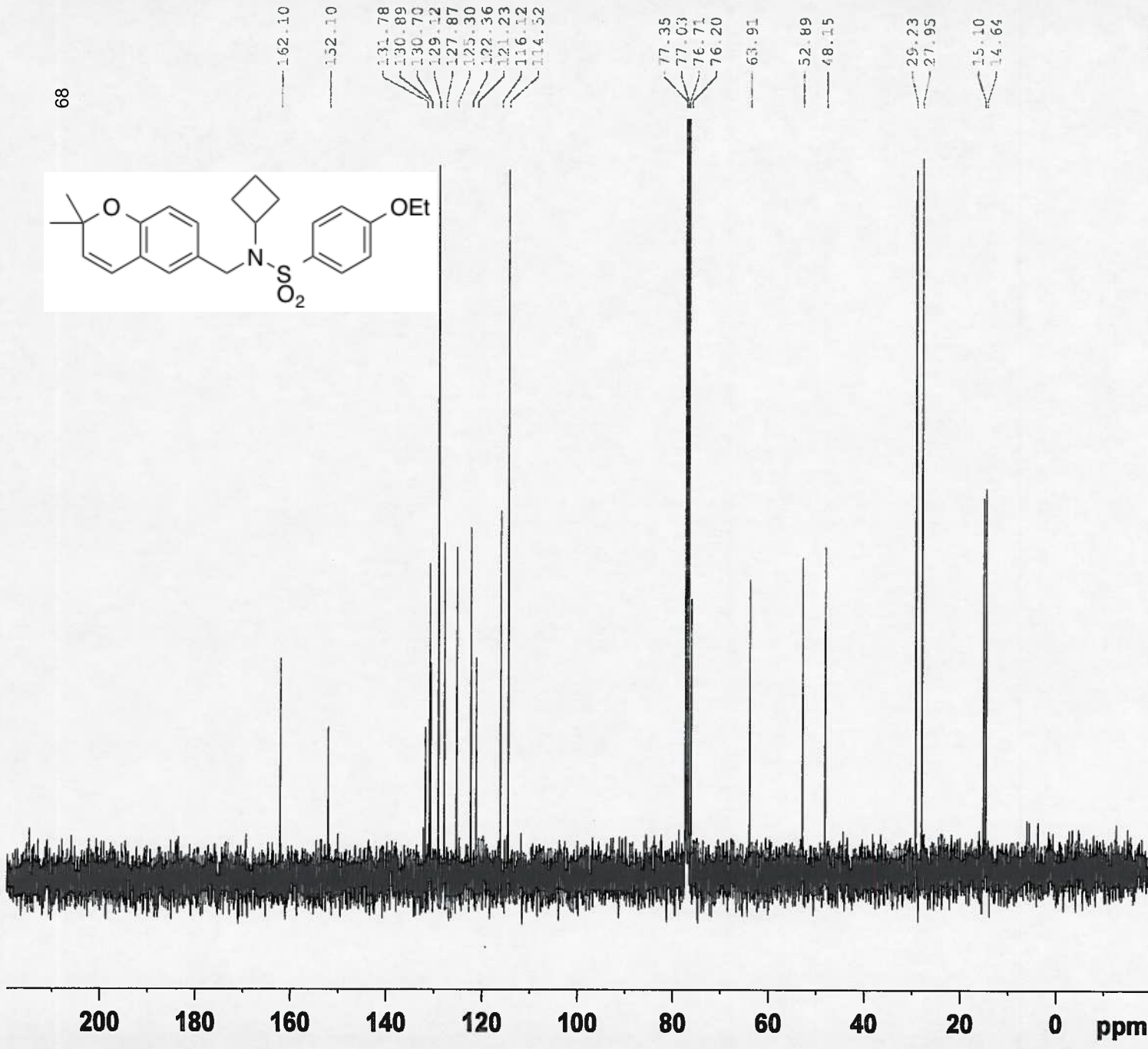
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400090 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDI-64c-13C



Current Data Parameters

NAME	ZDI-64c-13C
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20140209
Time	13.44
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	72
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	144
DW	20.800 usec
DE	6.50 usec
TE	298.3 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	100.6253441 MHz
NUC1	13C
P1	9.00 usec
PLW1	62.00000000 W

======== CHANNEL f2 ========

SFO2	400.1416006 MHz
NUC2	1H
CPDPRG[2	waltz16
PCPD2	90.00 usec
PLW2	16.00000000 W
PLW12	0.36000001 W
PLW13	0.29159999 W

F2 - Processing parameters

SI	32768
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

ZDI-82c

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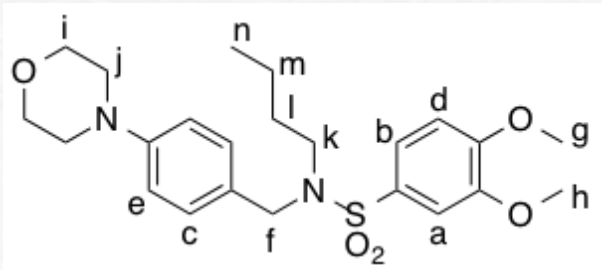

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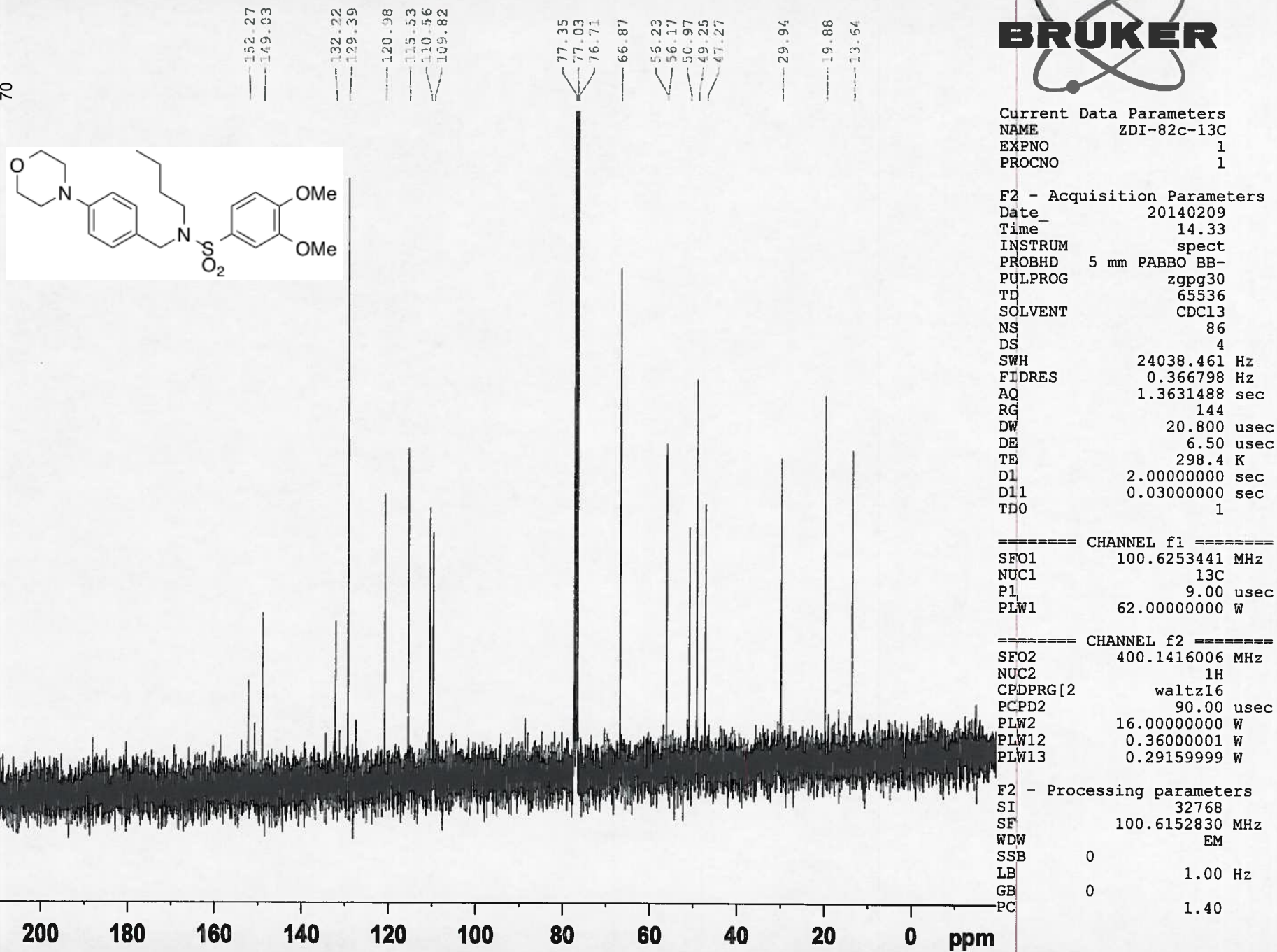
Current Data Parameters
NAME ZDI-82c
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140209
Time 14.26
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 128
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

ZDI-82c-13C



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Current Data Parameters

NAME	ZDI-82c-13C
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140209
Time	14.33
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	86
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	144
DW	20.800 usec
DE	6.50 usec
TE	298.4 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	100.6253441 MHz
NUC1	13C
P1	9.00 usec
PLW1	62.00000000 W

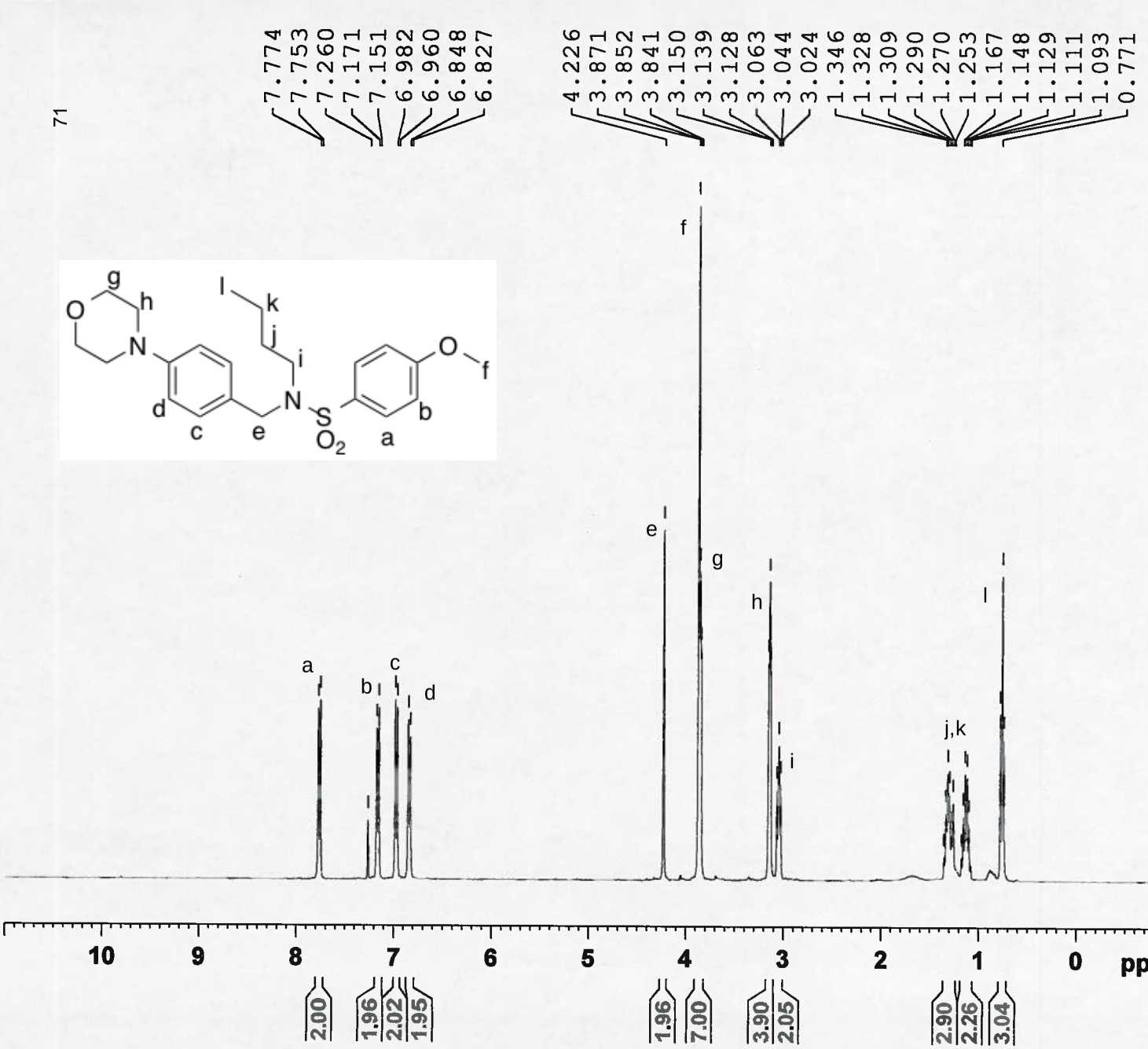
======== CHANNEL f2 ========

SFO2	400.1416006 MHz
NUC2	1H
CPDPRG[2	waltz16
PCPD2	90.00 usec
PLW2	16.00000000 W
PLW12	0.36000001 W
PLW13	0.29159999 W

F2 - Processing parameters

SI	32768
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

ZDI-88b



BRUKER

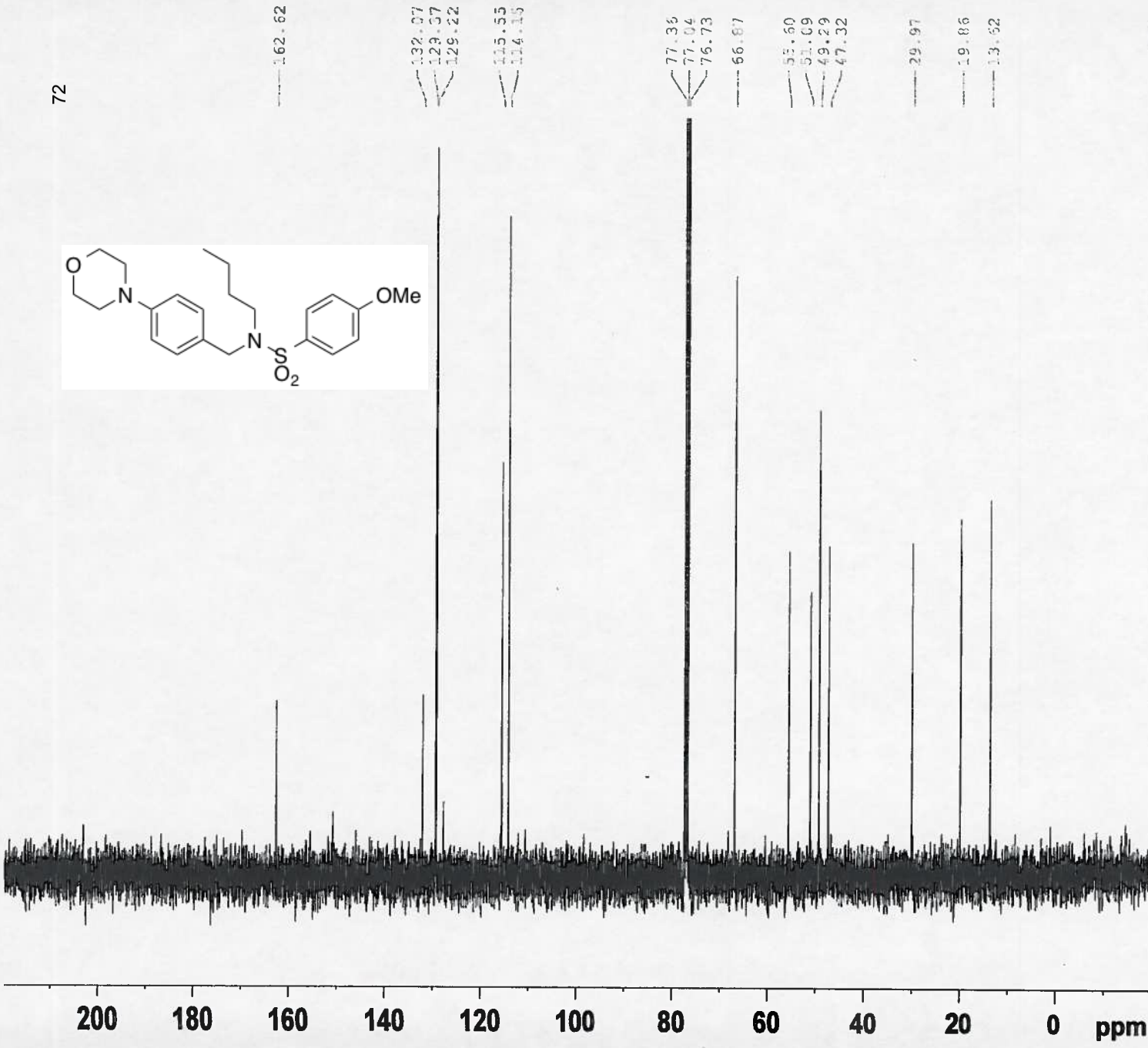
Current Data Parameters
NAME ZDI-70b
EXPNO 4
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140424
Time 16.38
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 80.6
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400082 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

ZDI-88b-13C



BRUKER

Current Data Parameters
NAME ZDI-70b-13C
EXPNO 4
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140424
Time 16.43
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 53
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 144
DW 20.800 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZD-I-83c

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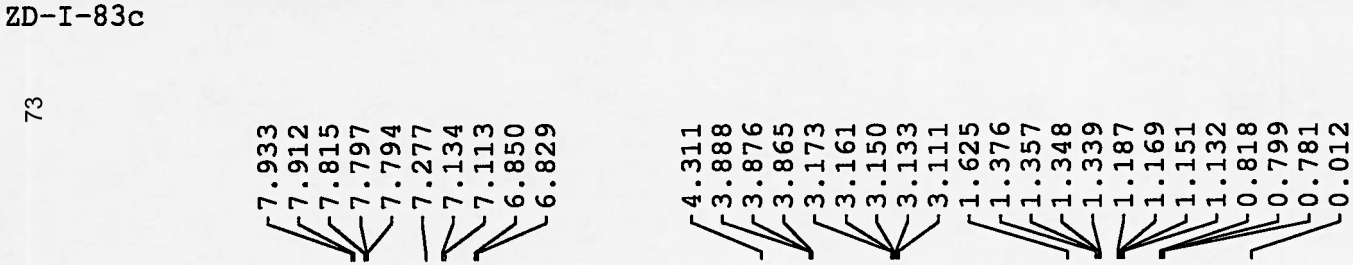

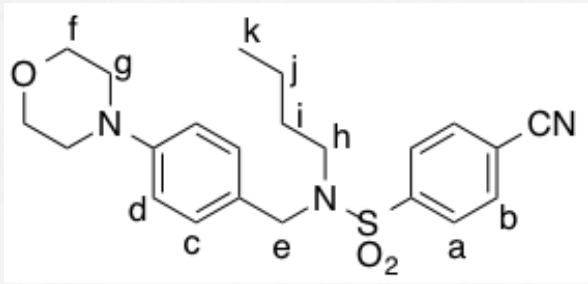

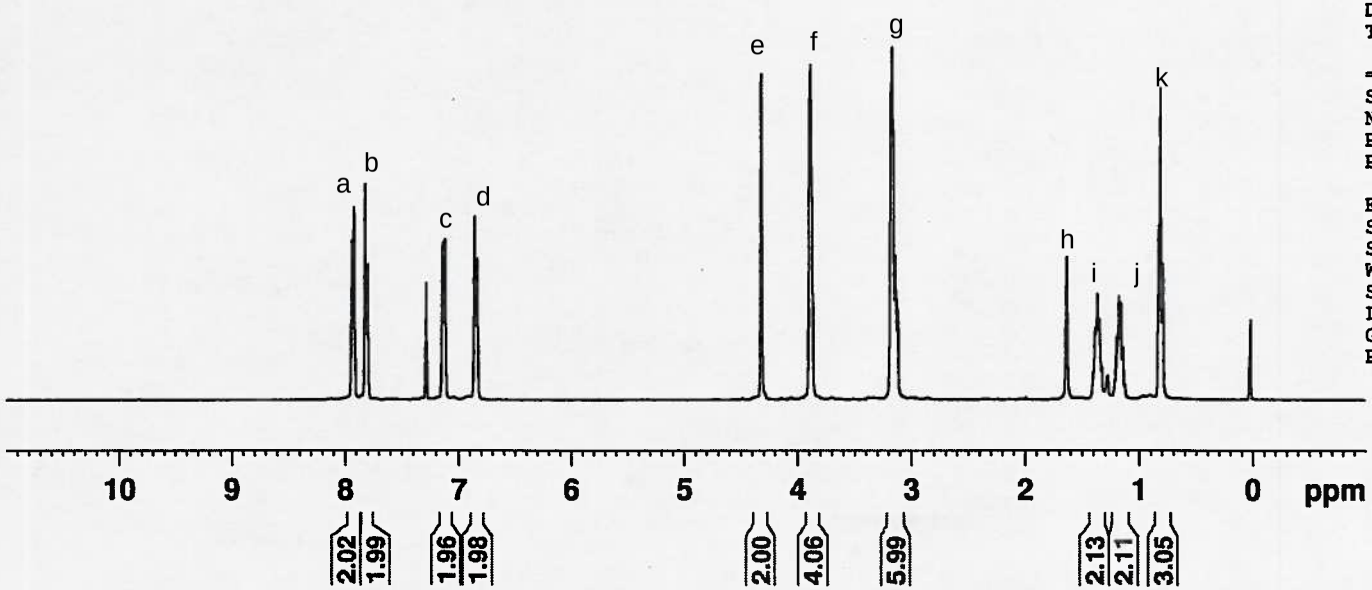

BRUKER

Current Data Parameters
NAME ZD-I-83c
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130315
Time 11.16
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 114
DW 62.400 usec
DE 6.50 usec
TE 293.8 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

ZD-I-83c

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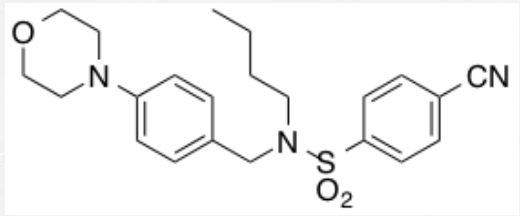

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Current Data Parameters
NAME ZD-I-83c
EXPNO 2
PROCNO 1

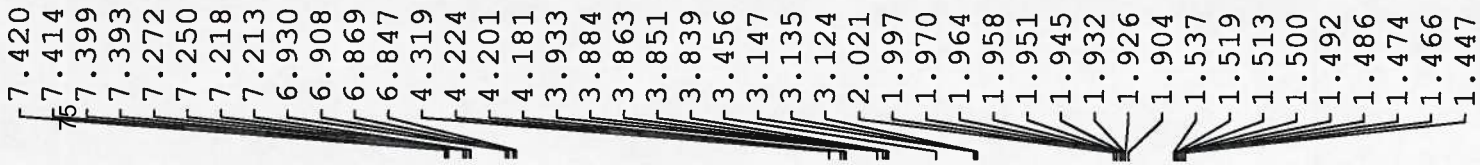
F2 - Acquisition Parameters
Date_ 20130315
Time 11.18
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 60
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 294.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

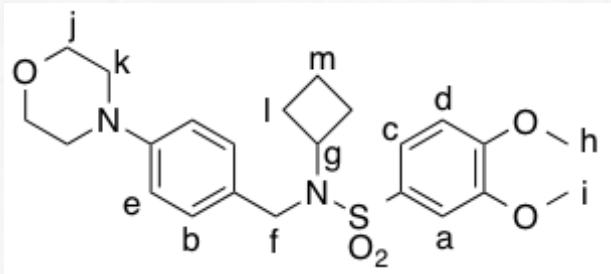
======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDII-27d





Current Data Parameters

NAME	ZDII-27d
EXPNO	5
PROCNO	1

F2 - Acquisition Parameters

Date_	20140527
Time	10.19
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	32
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

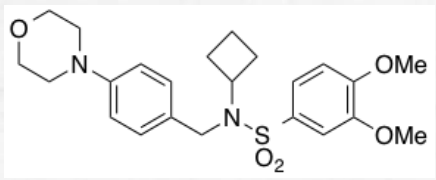
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1399986 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDII-27d-13C



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Current Data Parameters

NAME	ZDII-27d-13C
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20131109
Time	18.44
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	39
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	298.4 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	100.6253441 MHz
NUC1	13C
P1	9.00 usec
PLW1	62.00000000 W

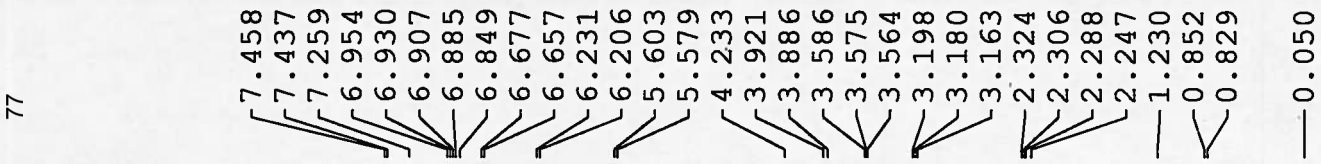
======== CHANNEL f2 ========

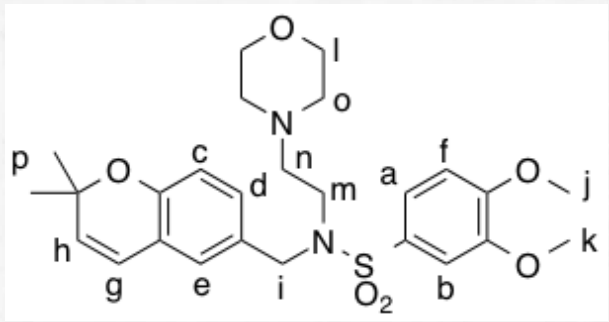
SFO2	400.1416006 MHz
NUC2	1H
CPDPRG[2	waltz16
PCPD2	90.00 usec
PLW2	16.00000000 W
PLW12	0.36000001 W
PLW13	0.29159999 W

F2 - Processing parameters

SI	32768
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

ZDII-55d





Current Data Parameters

NAME	ZDII-55d
EXPNO	4
PROCNO	1

F2 - Acquisition Parameters

Date_	20140109
Time	16.08
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	32
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

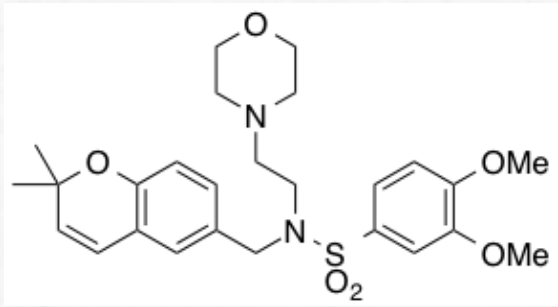
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400079 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDII-55d



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Current Data Parameters
NAME ZDII-55d-13C
EXPNO 5
PROCNO 1

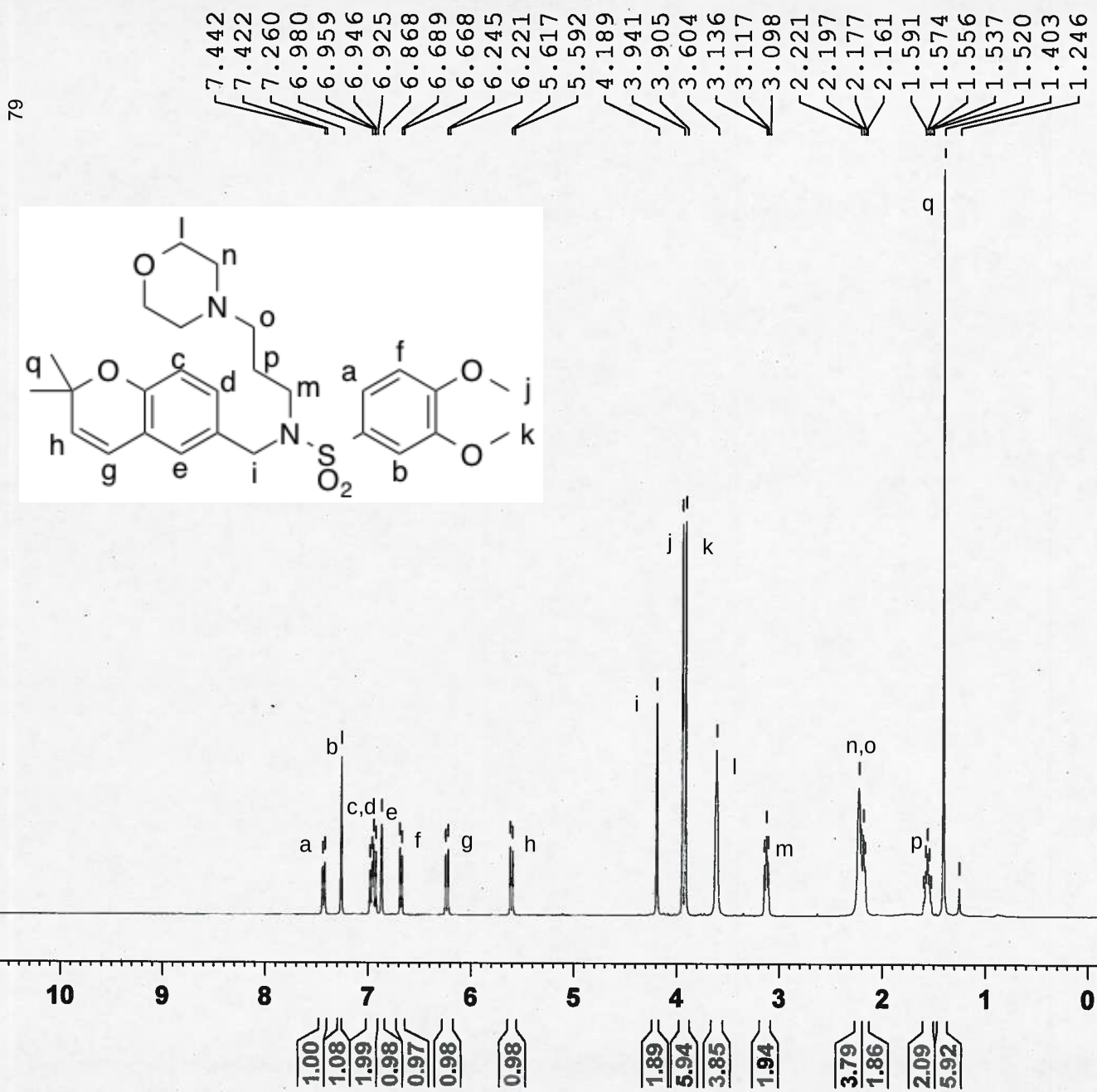
F2 - Acquisition Parameters
Date_ 20140110
Time 16.57
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 46
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDII-67d



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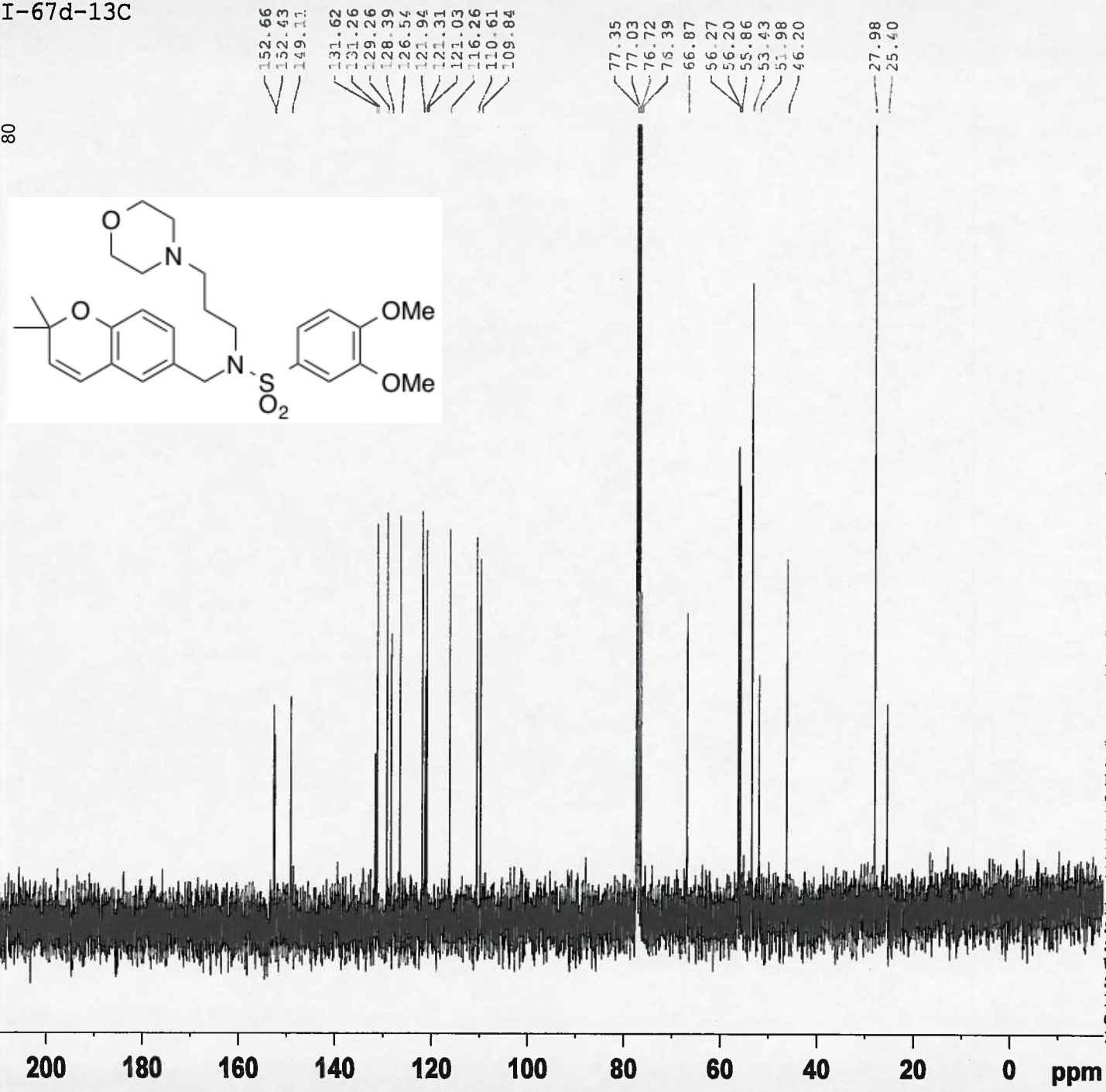
Current Data Parameters
NAME ZDII-67d
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140109
Time 16.19
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 101
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400087 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

ZDII-67d-13C



BRUKER

Current Data Parameters
NAME ZDII-67d-13C
EXPNO 3
PROCNO 1

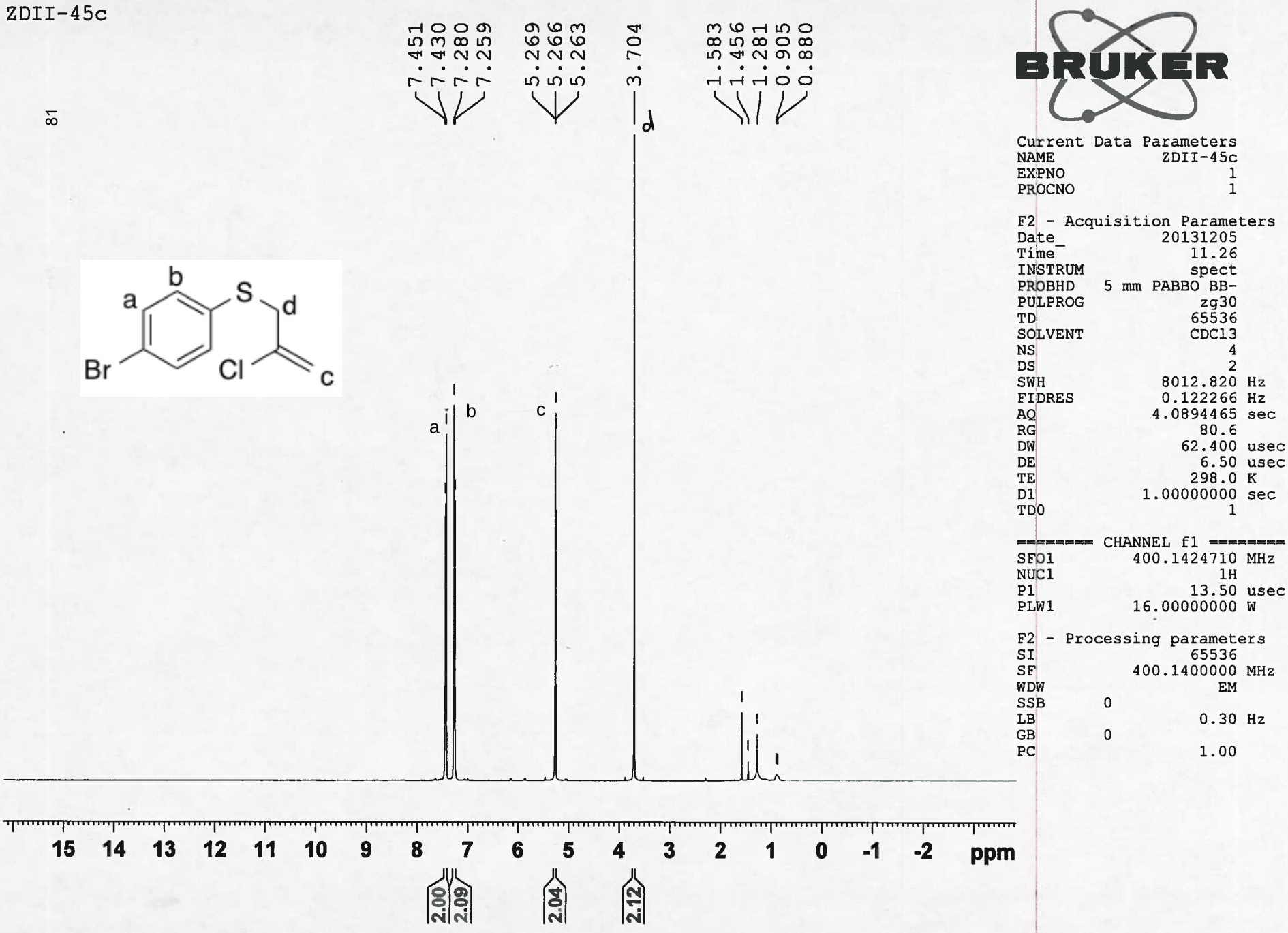
F2 - Acquisition Parameters
Date_ 20140109
Time 16.24
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 103
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 181
DW 20.800 usec
DE 6.50 usec
TE 298.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDII-45c



BRUKER

Current Data Parameters

NAME	ZDII-45c
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20131205
Time	11.26
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	4
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	80.6
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

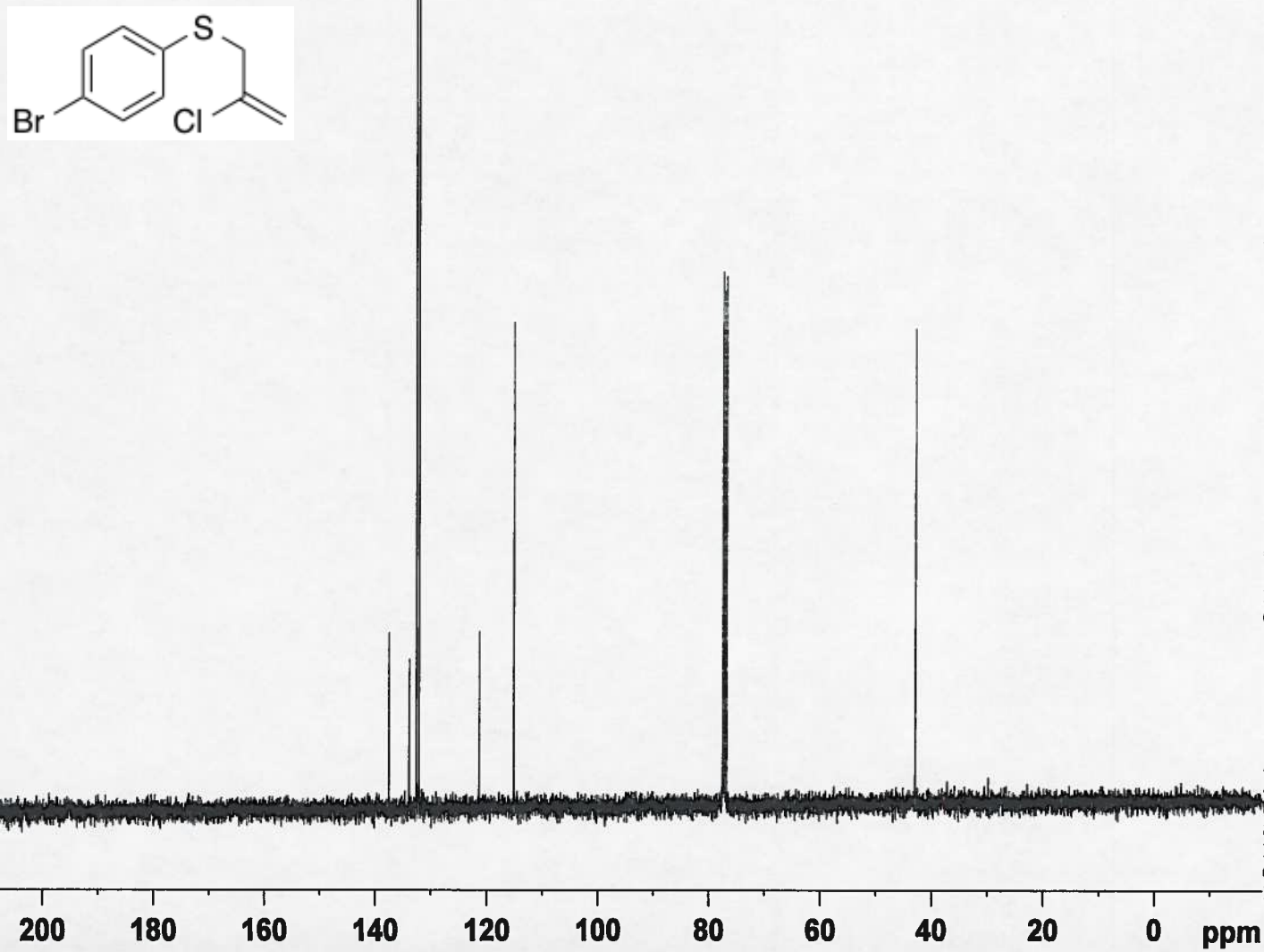
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDII-45c-13C



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Current Data Parameters
NAME ZDII-45c-13C
EXPNO 1
PROCNO 1

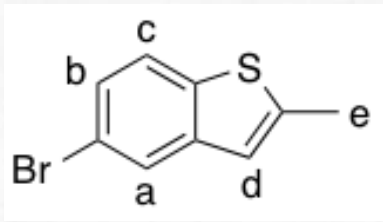
F2 - Acquisition Parameters
Date_ 20131205
Time 11.28
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 37
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 80.6
DW 20.800 usec
DE 6.50 usec
TE 298.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDII-57b



Current Data Parameters

NAME	ZDII-57b
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20140110
Time	17.05
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	128
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

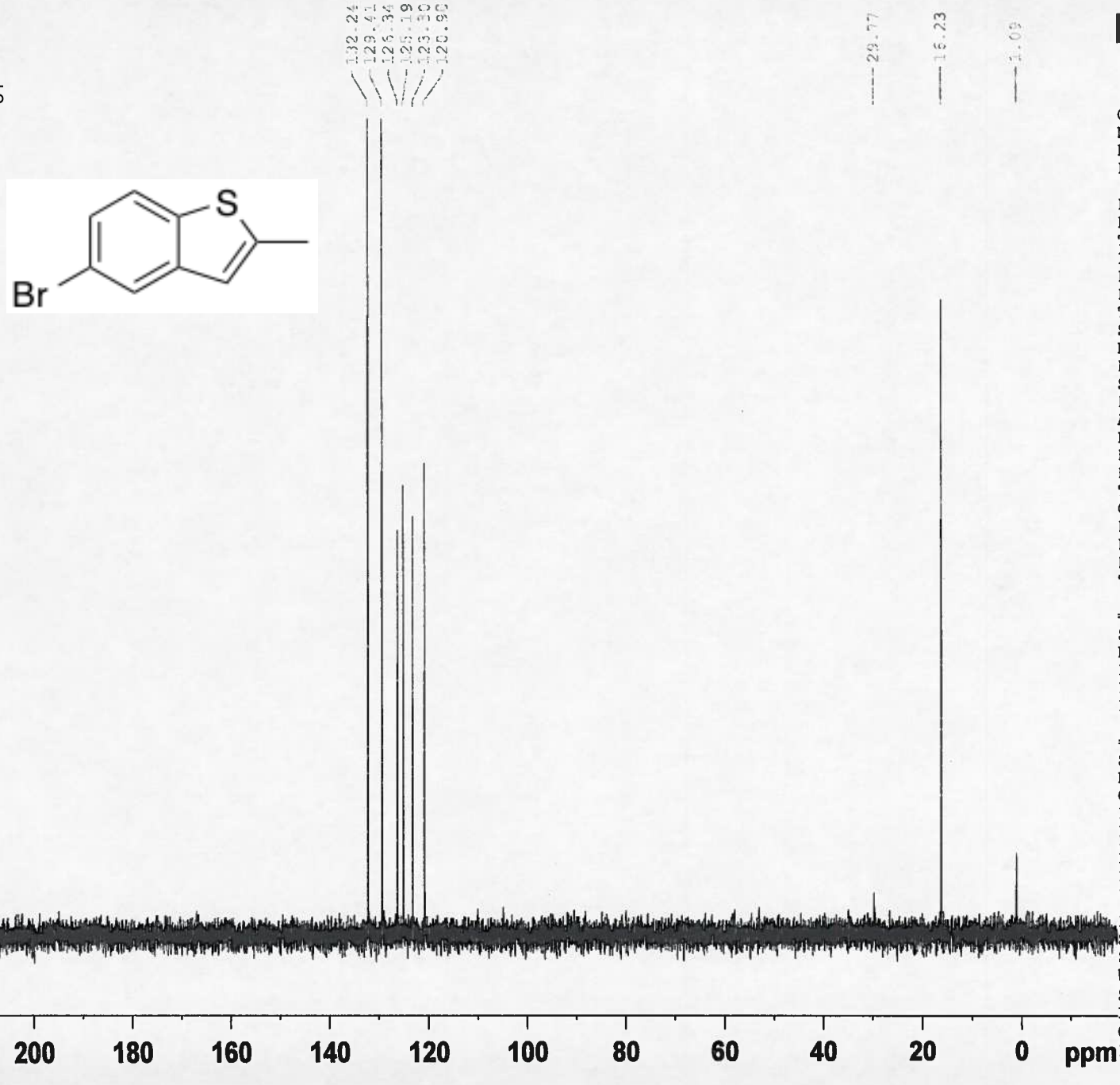
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400082 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDII-57b-13CDEPT



BRUKER

Current Data Parameters
NAME ZDII-57b-13CDEPT
EXPNO 1
PROCNO 1

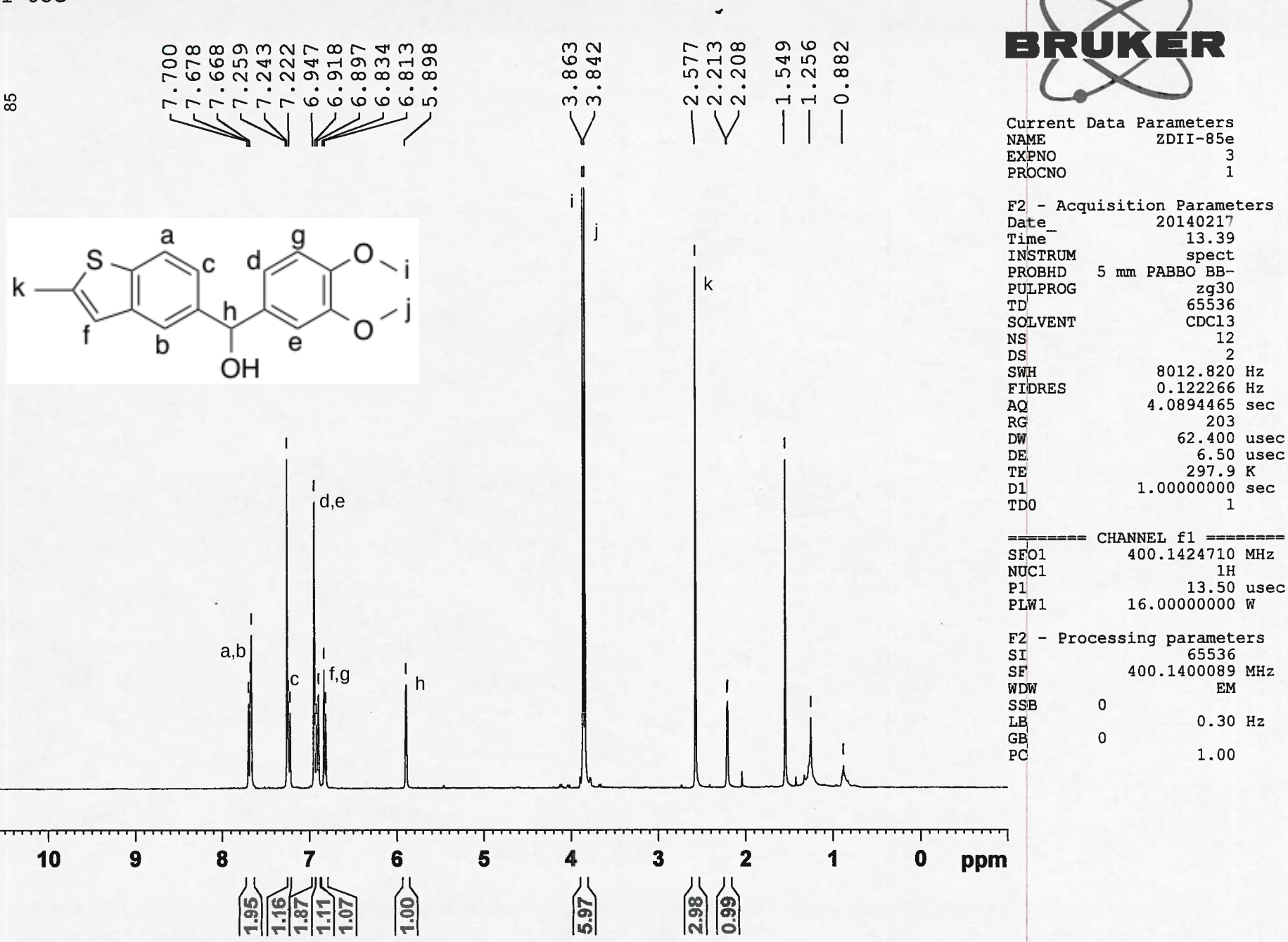
F2 - Acquisition Parameters
Date_ 20131216
Time 18.28
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG dept45
TD 65536
SOLVENT CDCl3
NS 24
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 298.2 K
CNST2 145.0000000
D1 2.00000000 sec
D2 0.00344828 sec
D12 0.00002000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253446 MHz
NUC1 13C
P1 9.00 usec
P2 18.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
P3 13.50 usec
P4 27.00 usec
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDII-85e



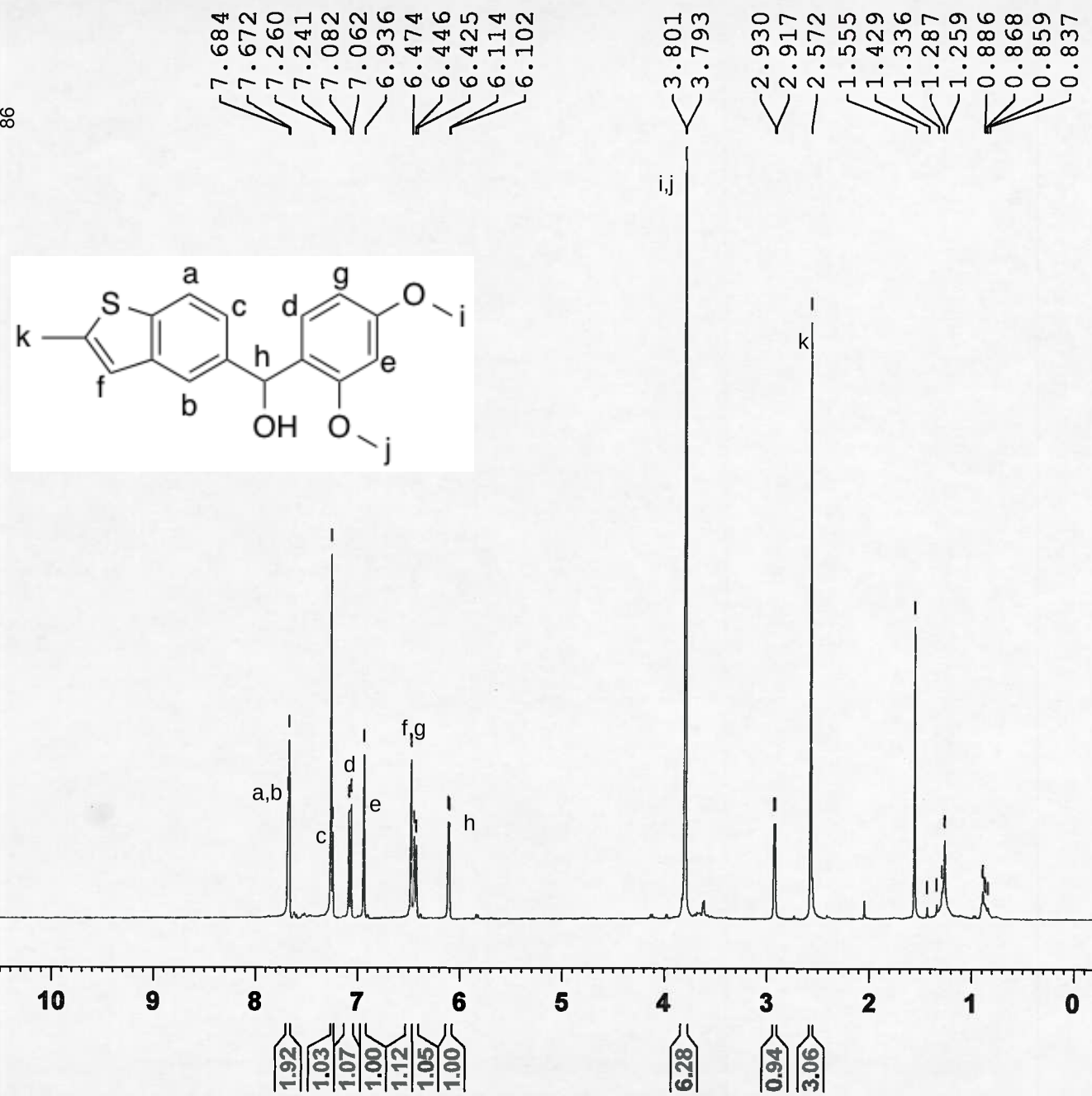

```
Current Data Parameters
NAME                  ZDII-85e
EXPNO                        3
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20140217
Time                     13.39
INSTRUM                  spect
PROBHD     5 mm PABBO BB-
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         12
DS                          2
SWH                   8012.820 Hz
FIDRES                0.122266 Hz
AQ                    4.0894465 sec
RG                        203
DW                     62.400 usec
DE                      6.50 usec
TE                     297.9 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1               400.1424710 MHz
NUC1                        1H
P1                      13.50 usec
PLW1              16.00000000 W

F2 - Processing parameters
SI                      65536
SF                 400.1400089 MHz
WDW                        EM
SSB                 0
LB                      0.30 Hz
GB                  0
PC                      1.00
```

ZDII-91d



BRUKER

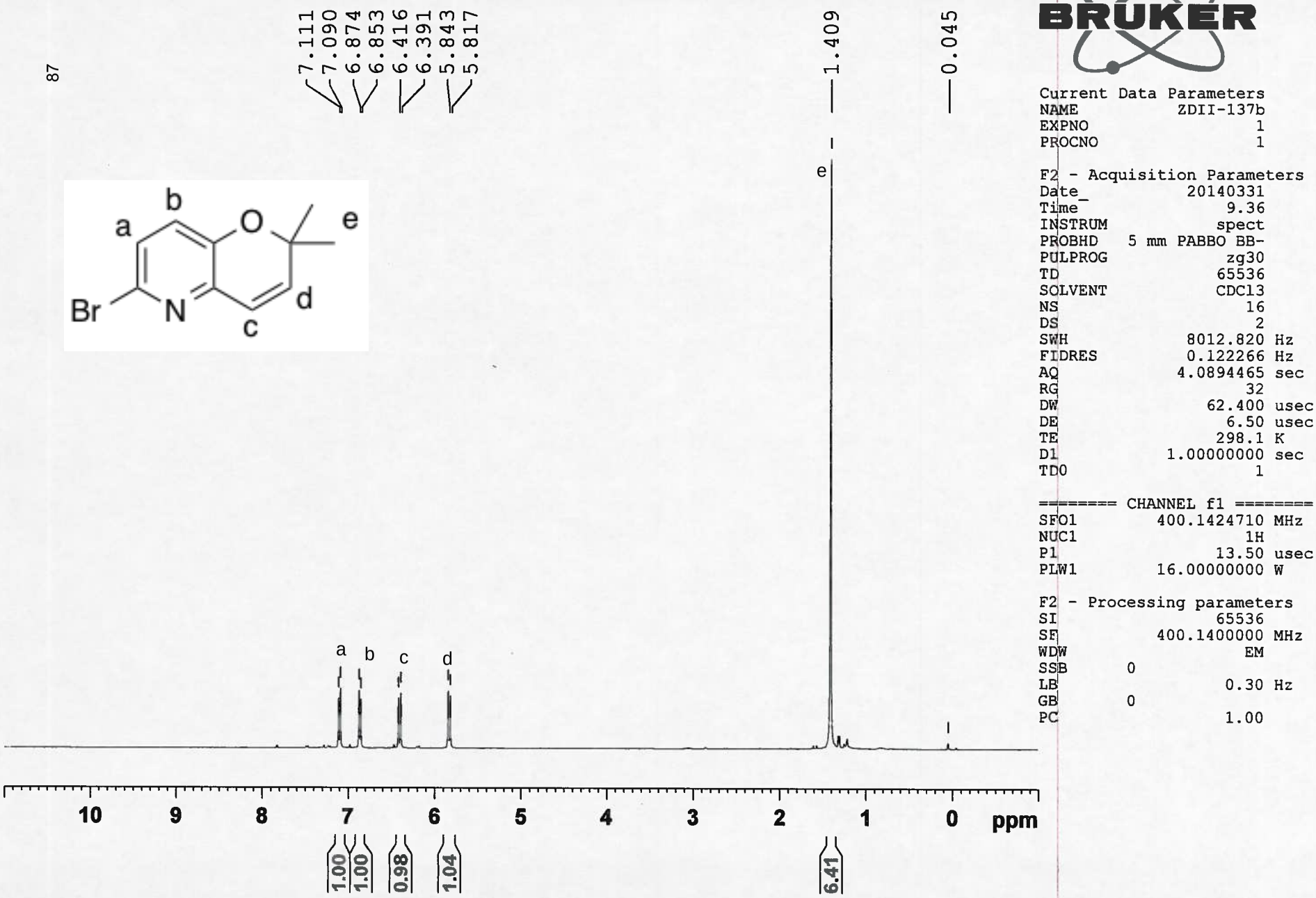
Current Data Parameters
NAME ZDII-91d
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140217
Time 13.48
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 203
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400090 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

ZDII-137b



BRUKER

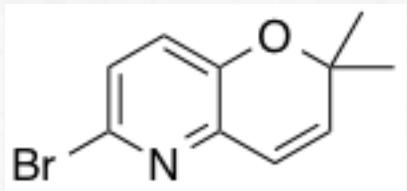
Current Data Parameters
NAME ZDII-137b
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140331
Time 9.36
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 32
DW 62.400 usec
DE 6.50 usec
TE 298.1 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

ZDII-137b-13C



BRUKER

Current Data Parameters
NAME ZDII-137b-13C
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140331
Time 9.40
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 49
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 161
DW 20.800 usec
DE 6.50 usec
TE 298.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDIII-35b

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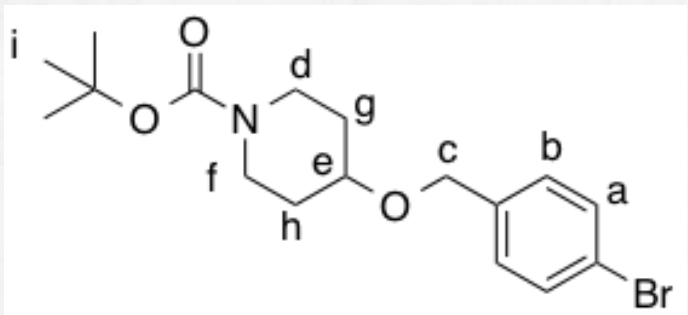
7.455 7.434 7.260 7.208 7.188 4.479 4.130 4.112 4.094 4.076 3.765 3.735 3.549 3.539 3.530 3.510 3.115 3.090 3.066 3.059 2.024 1.818 1.596 1.569 1.547 1.442 1.281 1.254 1.241 1.223 0.959 0.943



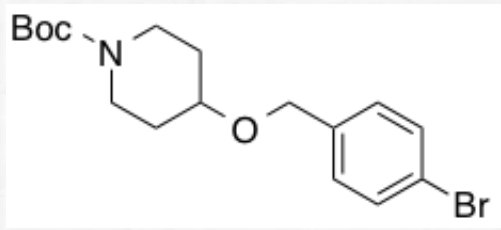
Current Data Parameters
NAME ZDIII-35b
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140513
Time 18.02
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 32
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400086 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

ZDIII-35b-13C



BRUKER

Current Data Parameters
NAME ZDIII-35b-13C
EXPNO 1
PROCNO 1

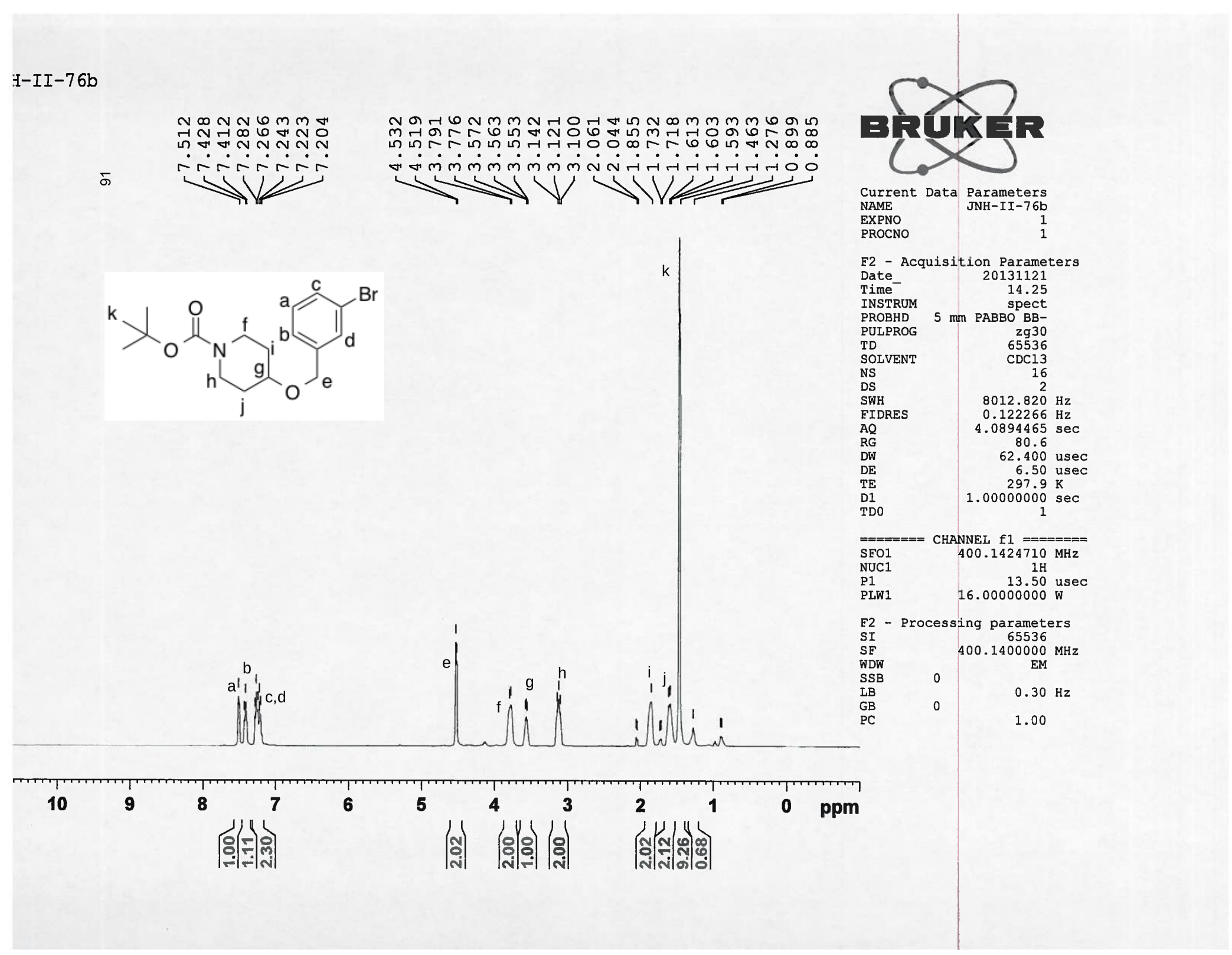
F2 - Acquisition Parameters
Date_ 20140513
Time 18.08
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 58
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 80.6
DW 20.800 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

H-II-76b



BRUKER

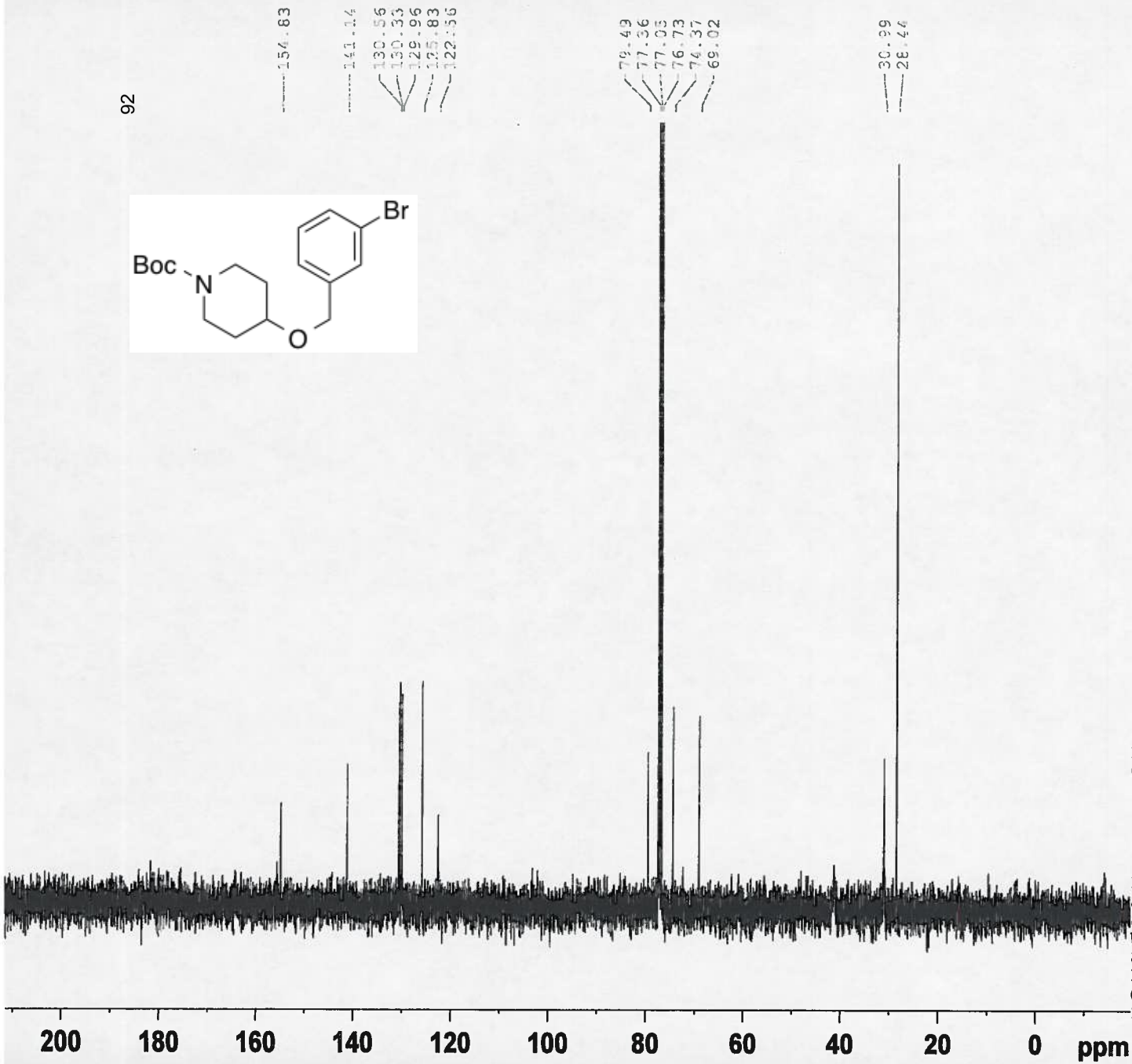
Current Data Parameters
NAME JNH-II-76b
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20131121
Time 14.25
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 80.6
DW 62.400 usec
DE 6.50 usec
TE 297.9 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

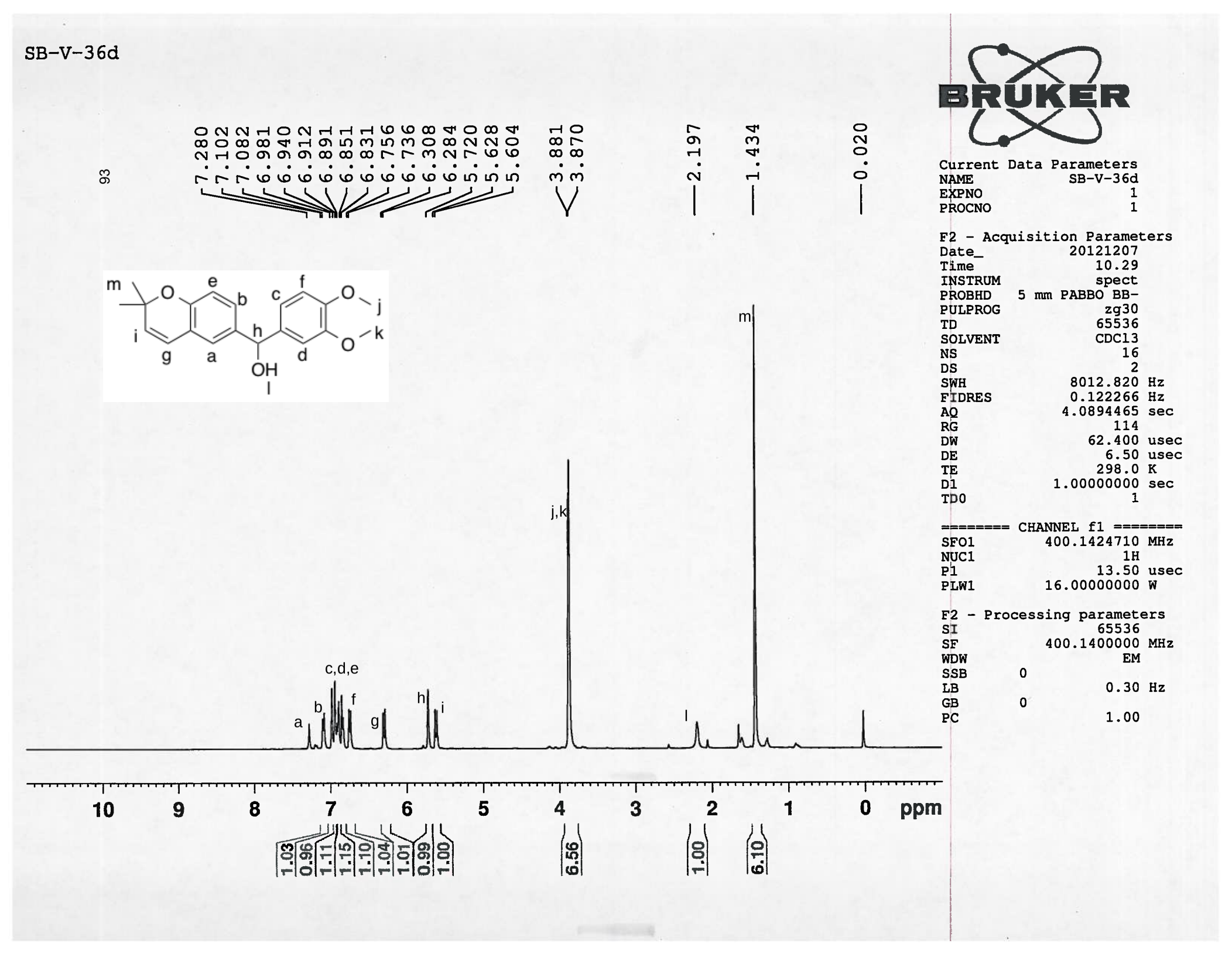
H-II-76b



BRUKER

```
Current Data Parameters
NAME          JNH-II-76b
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20131121
Time              14.30
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                   40
DS                    4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631488 sec
RG                  203
DW               20.800 usec
DE                6.50 usec
TE                298.1 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1         100.6253441 MHz
NUC1                13C
P1                9.00 usec
PLW1         62.00000000 W

======== CHANNEL f2 ========
SFO2         400.1416006 MHz
NUC2                1H
CPDPRG[2        waltz16
PCPD2            90.00 usec
PLW2         16.00000000 W
PLW12         0.36000001 W
PLW13         0.29159999 W

F2 - Processing parameters
SI                 32768
SF           100.6152830 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

SB-V-36d



Current Data Parameters

NAME	SB-V-36d
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20121207
Time	10.29
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	114
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

SB-V-36d

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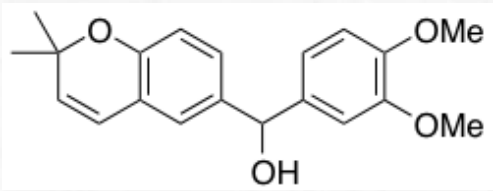
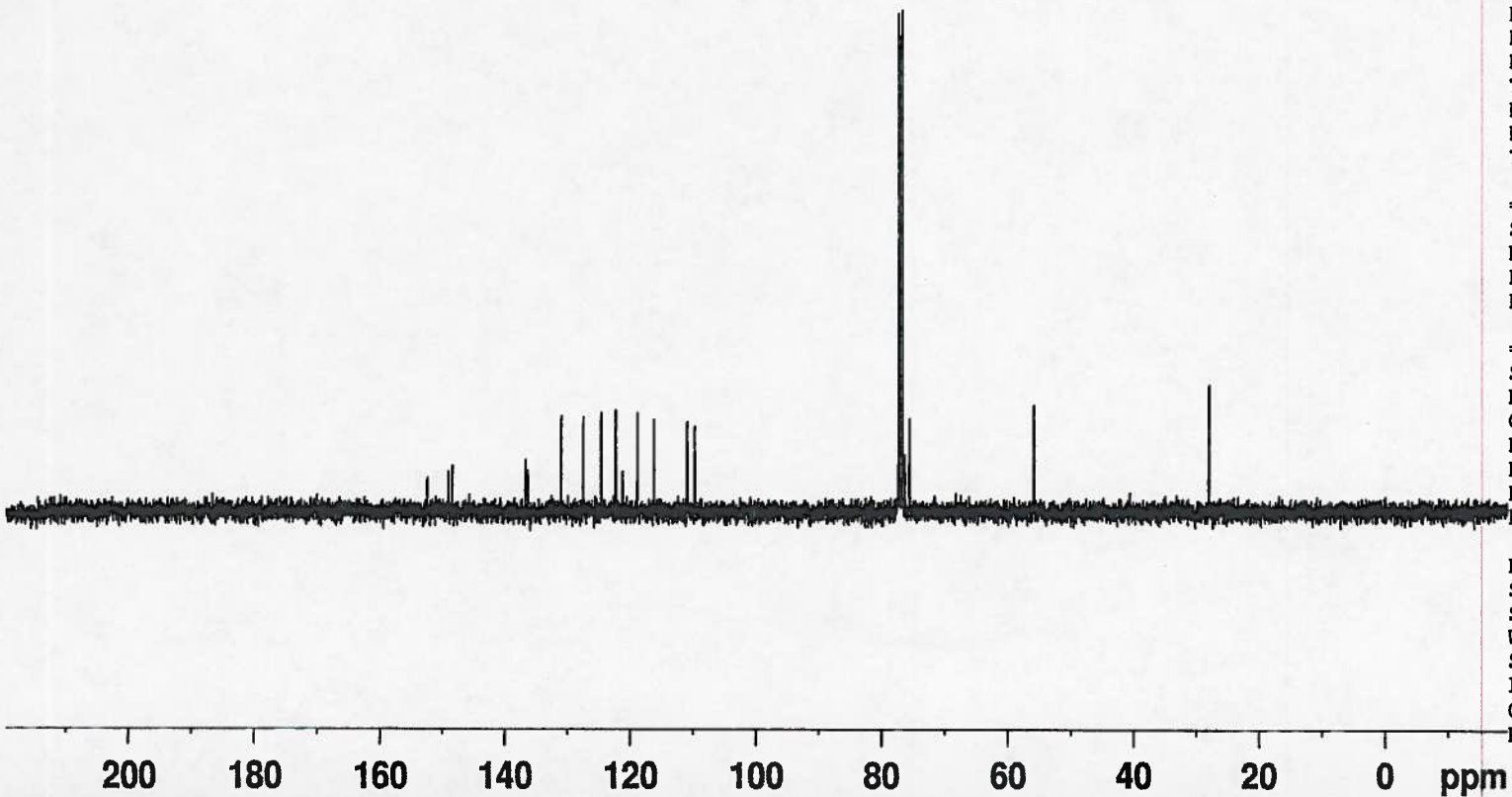




BRUKER

Current Data Parameters
NAME SB-V-36d
EXPNO 2
PROCNO 1

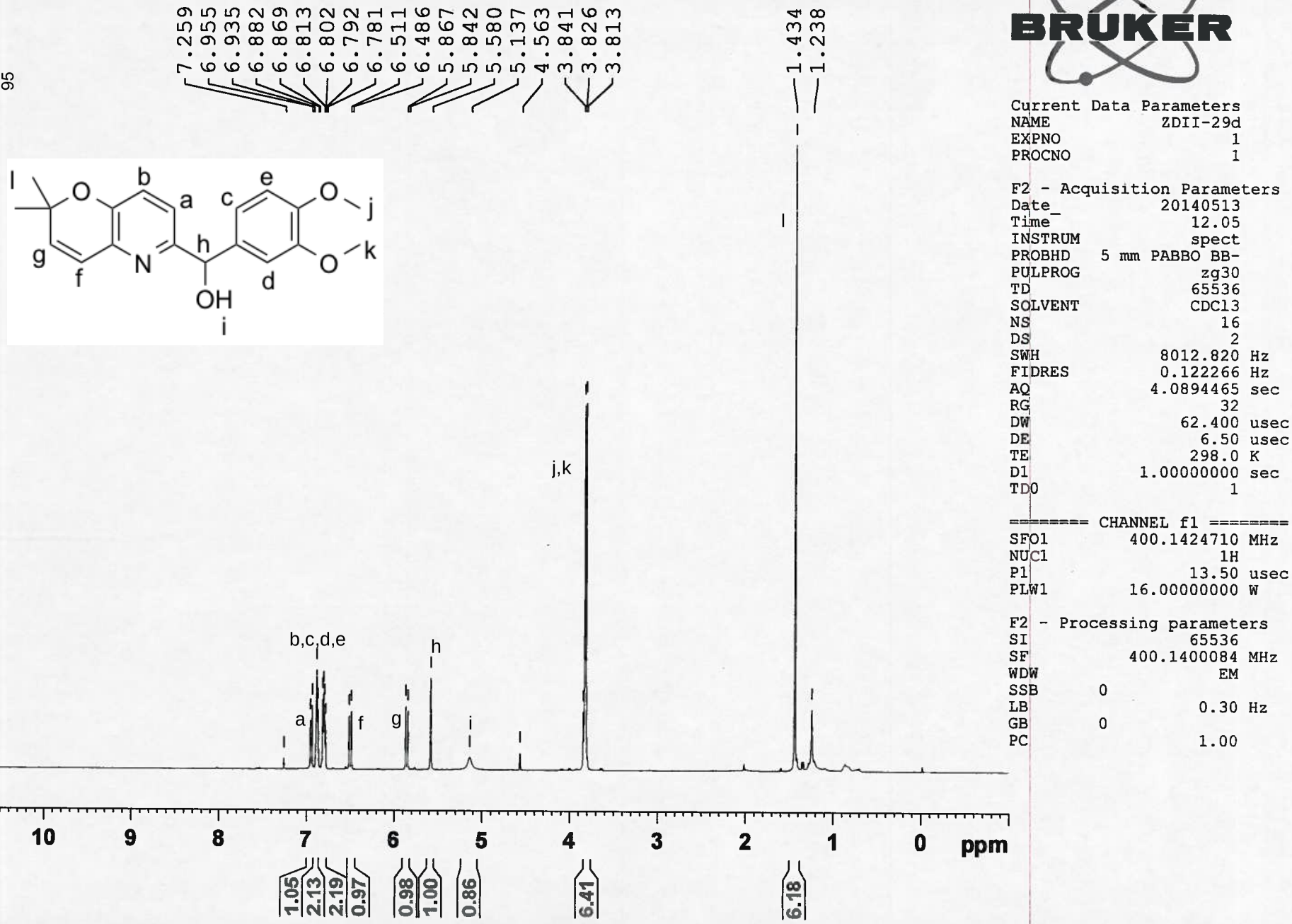
F2 - Acquisition Parameters
Date_ 20121207
Time 10.33
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 41
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 298.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDIII-29d



Current Data Parameters

NAME	ZDII-29d
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140513
Time	12.05
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	32
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

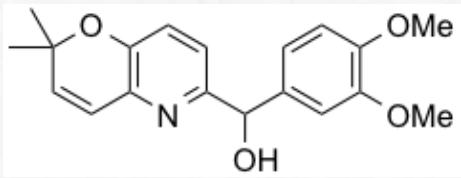
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400084 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

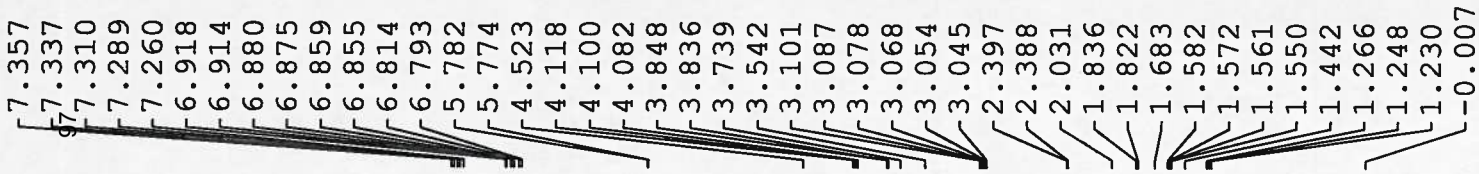
ZDII-29d-13C

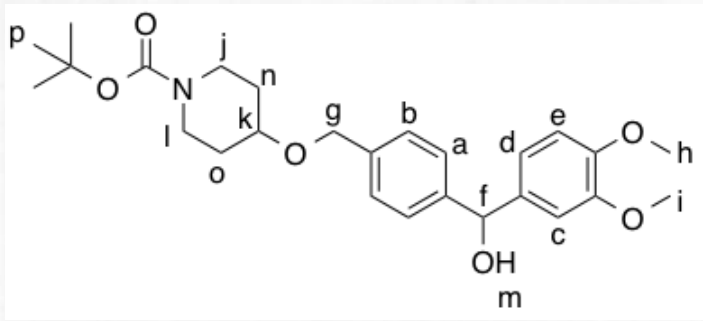


BRUKER

```
Current Data Parameters
NAME        ZDII-29d-13C
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140513
Time              12.17
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                  117
DS                    4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631488 sec
RG                  203
DW               20.800 usec
DE                6.50 usec
TE                298.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        100.6253441 MHz
NUC1                13C
P1                9.00 usec
PLW1        62.00000000 W

======== CHANNEL f2 ========
SFO2        400.1416006 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2        16.00000000 W
PLW12        0.36000001 W
PLW13        0.29159999 W

F2 - Processing parameters
SI                 32768
SF          100.6152830 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

ZDIII-43d





Current Data Parameters

NAME	ZDIII-43d
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140515
Time	11.37
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	90.5
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400084 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDIII-43d-13C

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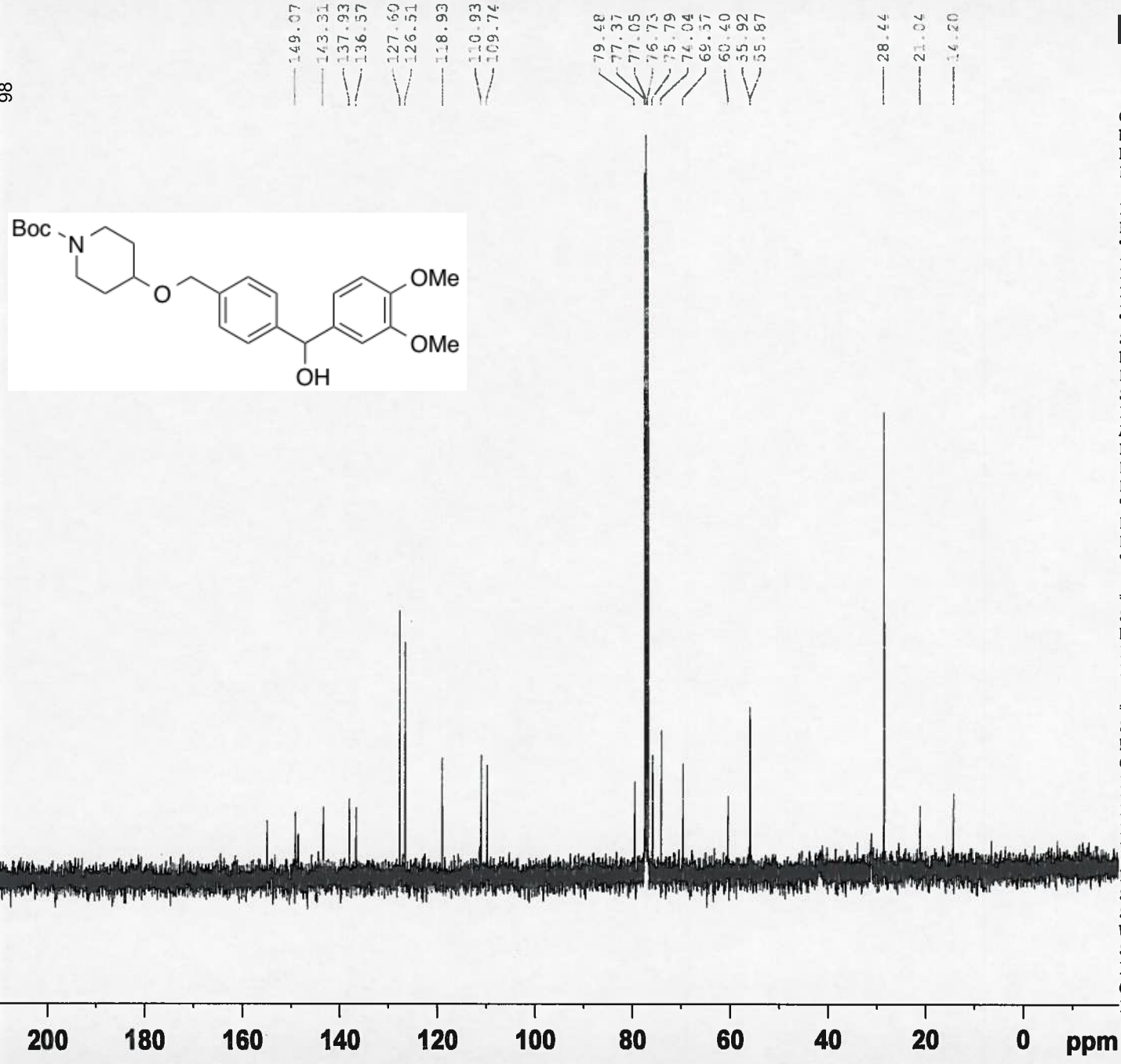


BRUKER

Current Data Parameters
NAME ZDIII-43d-13C
EXPNO 1
PROCNO 1

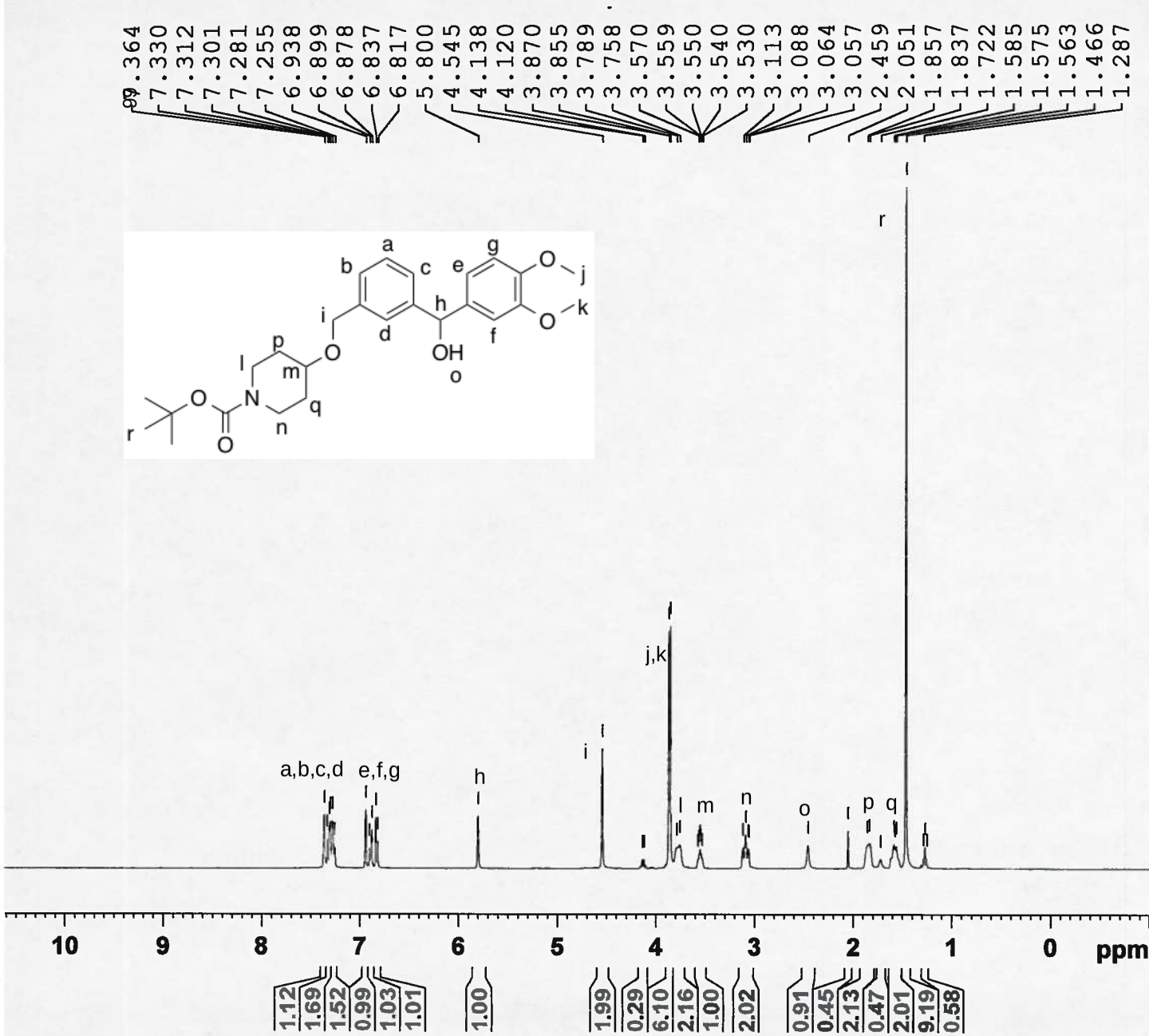
F2 - Acquisition Parameters
Date_ 20140515
Time 11.45
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 48
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 57
DW 20.800 usec
DE 6.50 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

H-II-100cb



Current Data Parameters

NAME	JNH-II-100cb
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140130
Time	12.32
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	71.8
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

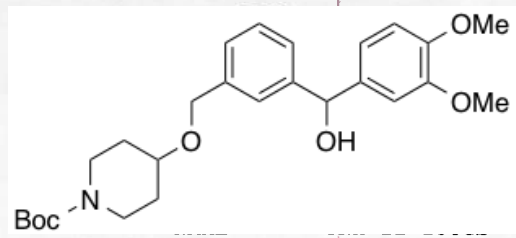
======== CHANNEL f1 ========

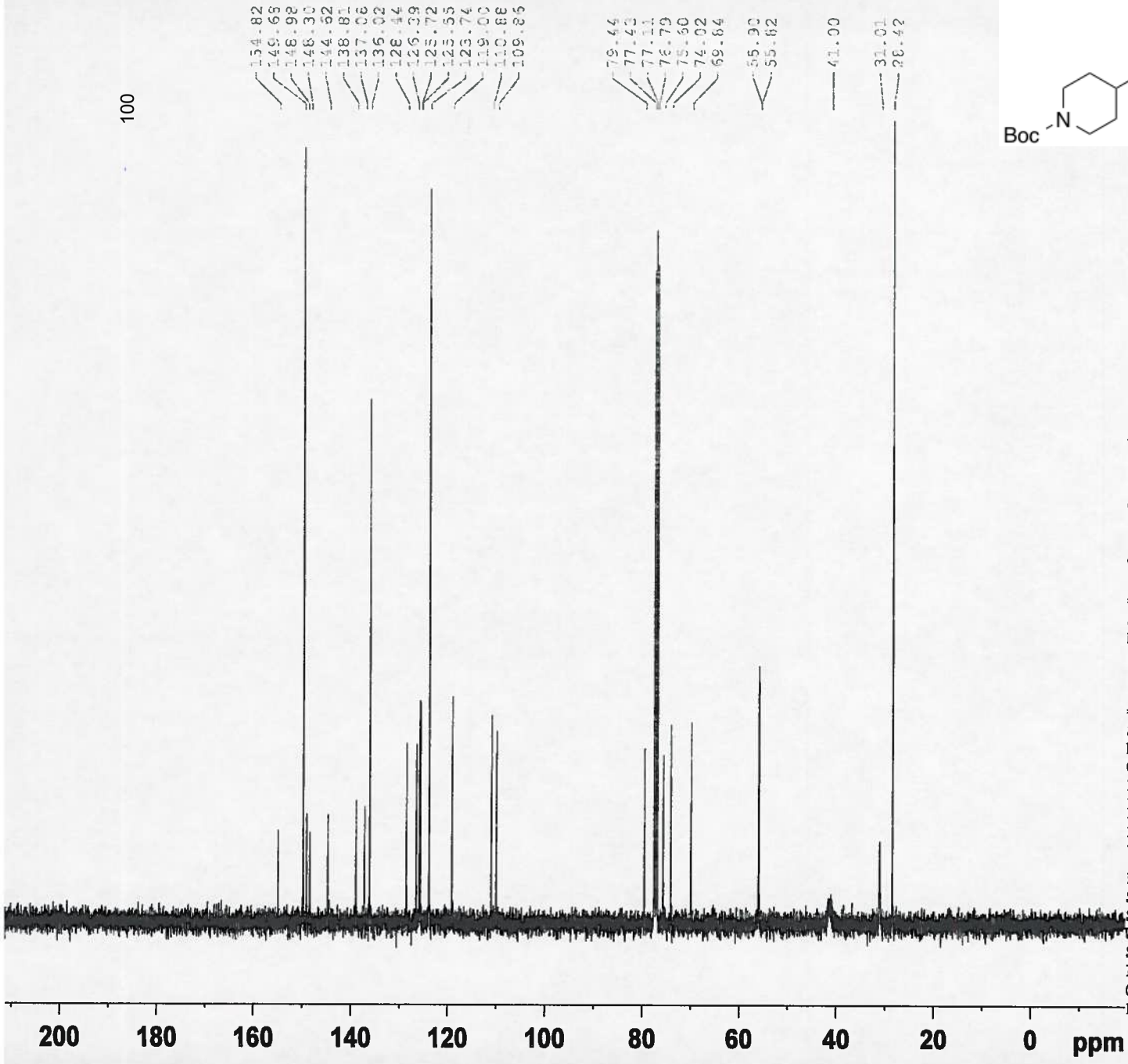
SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

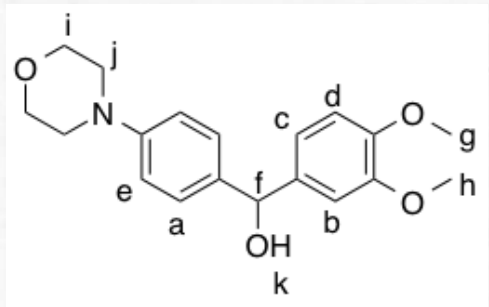
H-II-100cb





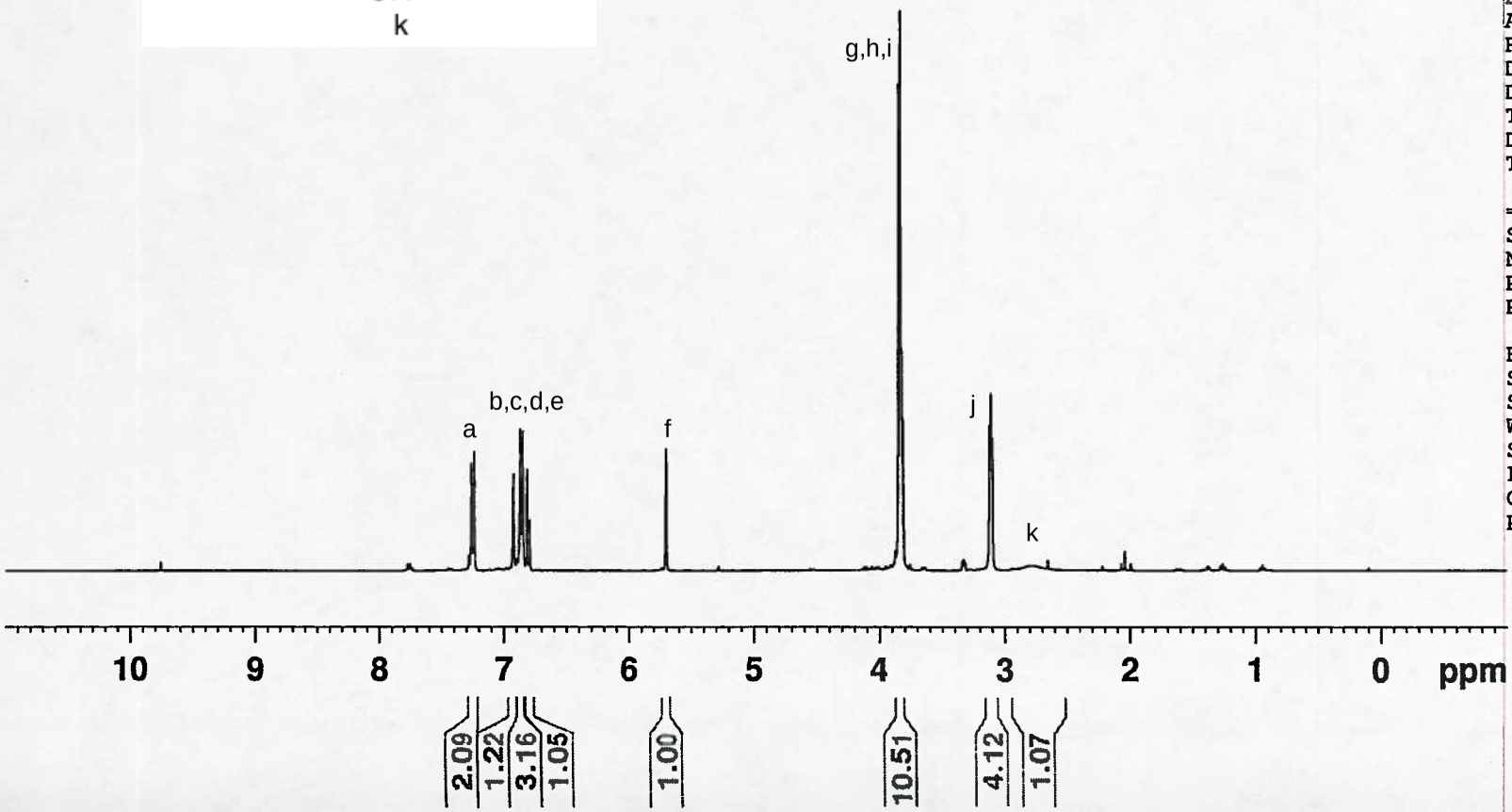
EXPNO	7	
PROCNO	1	
F2 - Acquisition Parameters		
Date_	20140404	
Time	9.25	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	59	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631488	sec
RG	114	
DW	20.800	usec
DE	6.50	usec
TE	298.4	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
SFO1	100.6253441	MHz
NUC1	13C	
P1	9.00	usec
PLW1	62.00000000	W
======== CHANNEL f2 ========		
SFO2	400.1416006	MHz
NUC2	1H	
CPDPRG[2	waltz16	
PCPD2	90.00	usec
PLW2	16.00000000	W
PLW12	0.36000001	W
PLW13	0.29159999	W
F2 - Processing parameters		
SI	32768	
SF	100.6152804	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

SB-V-102d



101

7.261
7.239
6.924
6.870
6.850
6.815
6.795
5.703
3.850
3.834
3.815
3.123
3.111
3.099



BRUKER

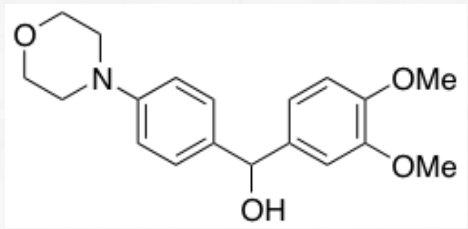
Current Data Parameters
NAME SB-V-102d
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130311
Time 22.29
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 13
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 28.5
DW 62.400 usec
DE 6.50 usec
TE 294.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

F2 - Processing parameters
SI 65536
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

SB-V-102d



102

Current Data Parameters

NAME	SB-V-102d
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20130311
Time	22.34
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	29
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	100.6253441 MHz
NUC1	13C
P1	9.00 usec
PLW1	62.00000000 W

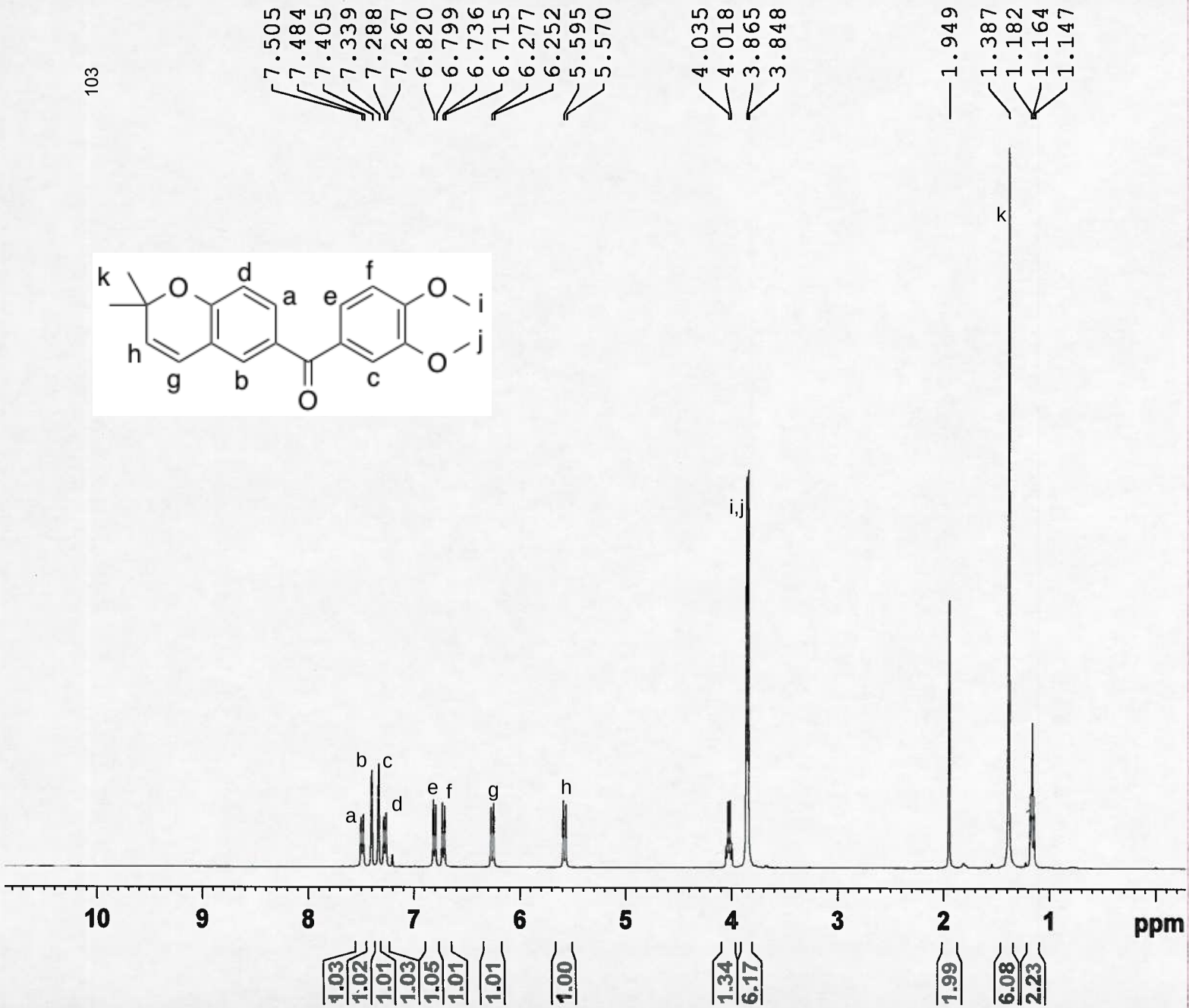
======== CHANNEL f2 ========

SFO2	400.1416006 MHz
NUC2	1H
CPDPRG[2	waltz16
PCPD2	90.00 usec
PLW2	16.00000000 W
PLW12	0.36000001 W
PLW13	0.29159999 W

F2 - Processing parameters

SI	32768
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

ZDII-95b 1H



Current Data Parameters

NAME	ZDII-95b 1H
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140225
Time	15.04
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	32
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

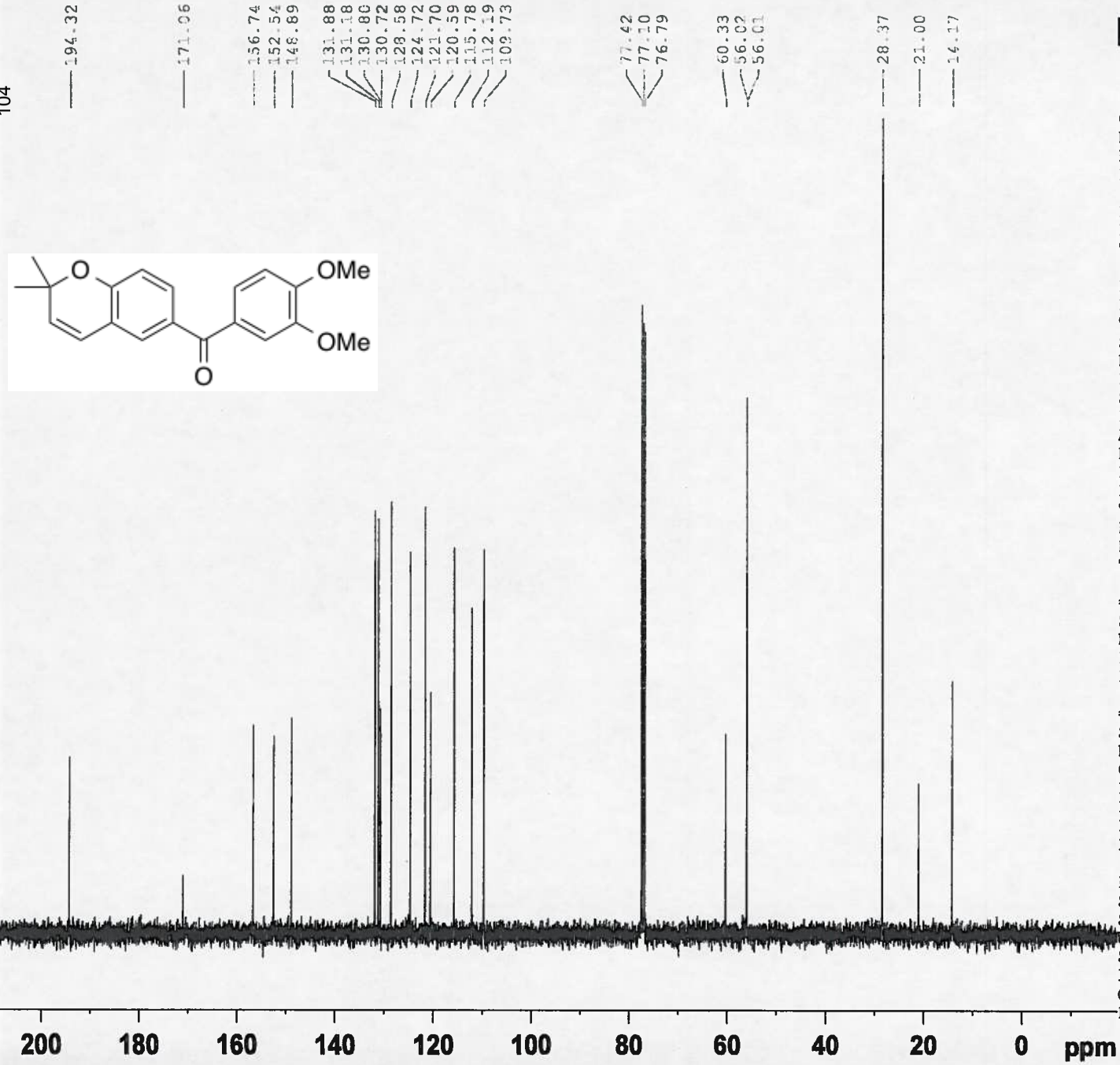
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400286 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDII-95b 13C



BRUKER

Current Data Parameters
NAME ZDII-95b 1H
EXPNO 2
PROCNO 1

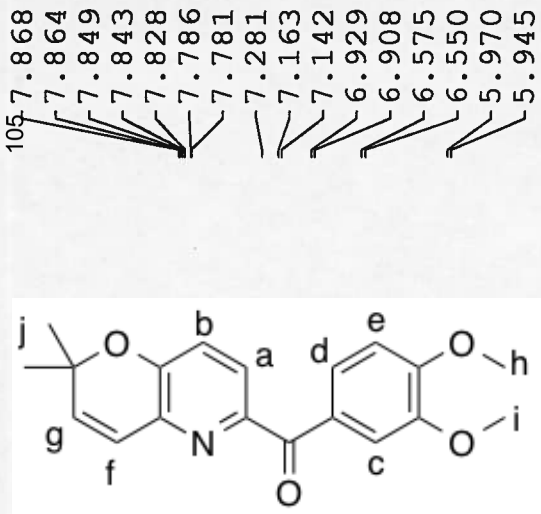
F2 - Acquisition Parameters
Date_ 20140225
Time 15.10
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 33
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 181
DW 20.800 usec
DE 6.50 usec
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDIII-73b



Current Data Parameters

NAME	ZDIII-73b
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140527
Time	10.03
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	80.6
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

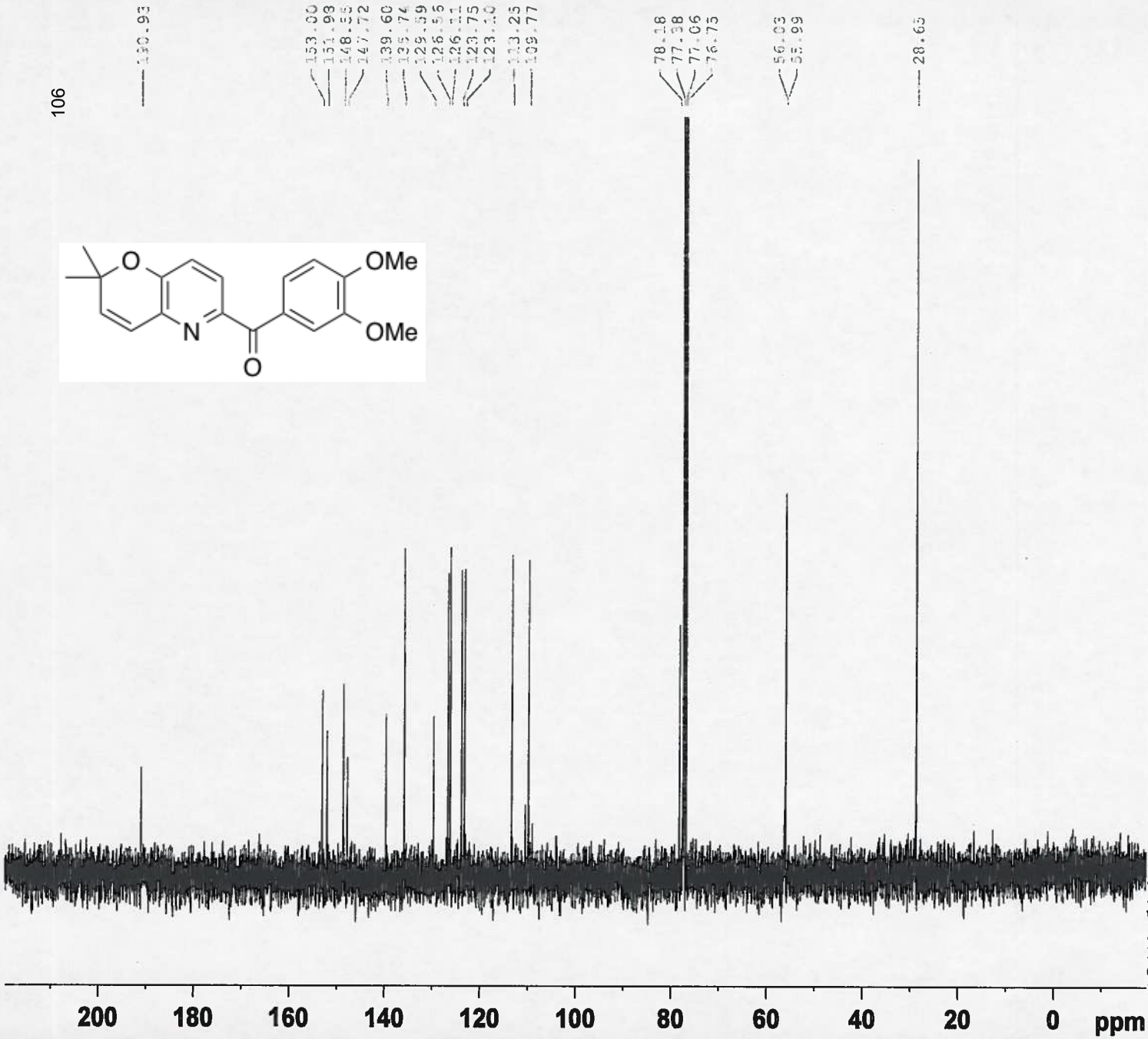
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDIII-73b-13C



BRUKER

Current Data Parameters

NAME	ZDIII-73b-13C
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140527
Time	10.08
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	27
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	90.5
DW	20.800 usec
DE	6.50 usec
TE	298.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	100.6253441 MHz
NUC1	13C
P1	9.00 usec
PLW1	62.00000000 W

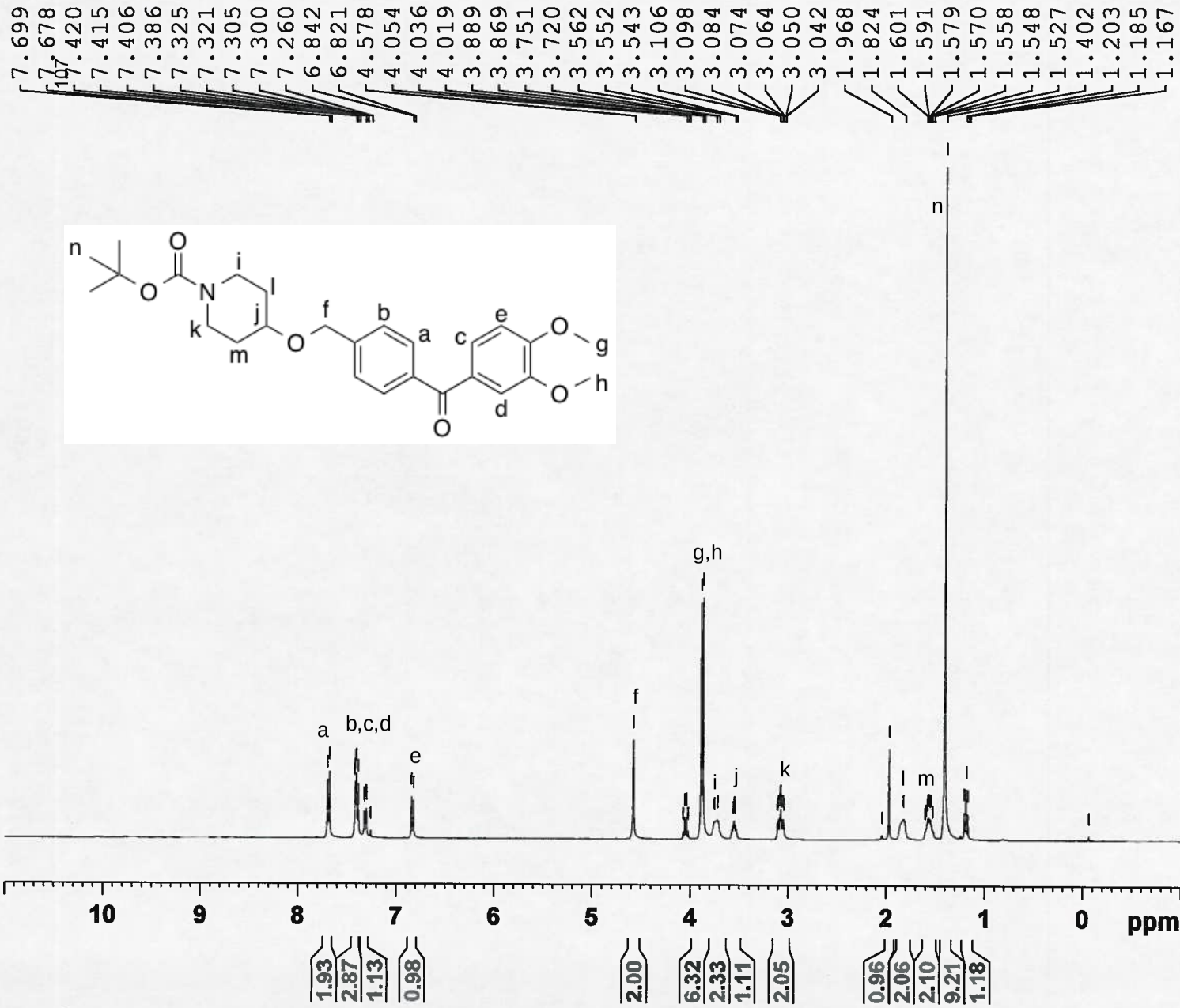
======== CHANNEL f2 ========

SFO2	400.1416006 MHz
NUC2	1H
CPDPRG[2	waltz16
PCPD2	90.00 usec
PLW2	16.00000000 W
PLW12	0.36000001 W
PLW13	0.29159999 W

F2 - Processing parameters

SI	32768
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

ZDIII-47c



Current Data Parameters

NAME	ZDIII-47c
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140515
Time	18.10
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	20.2
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

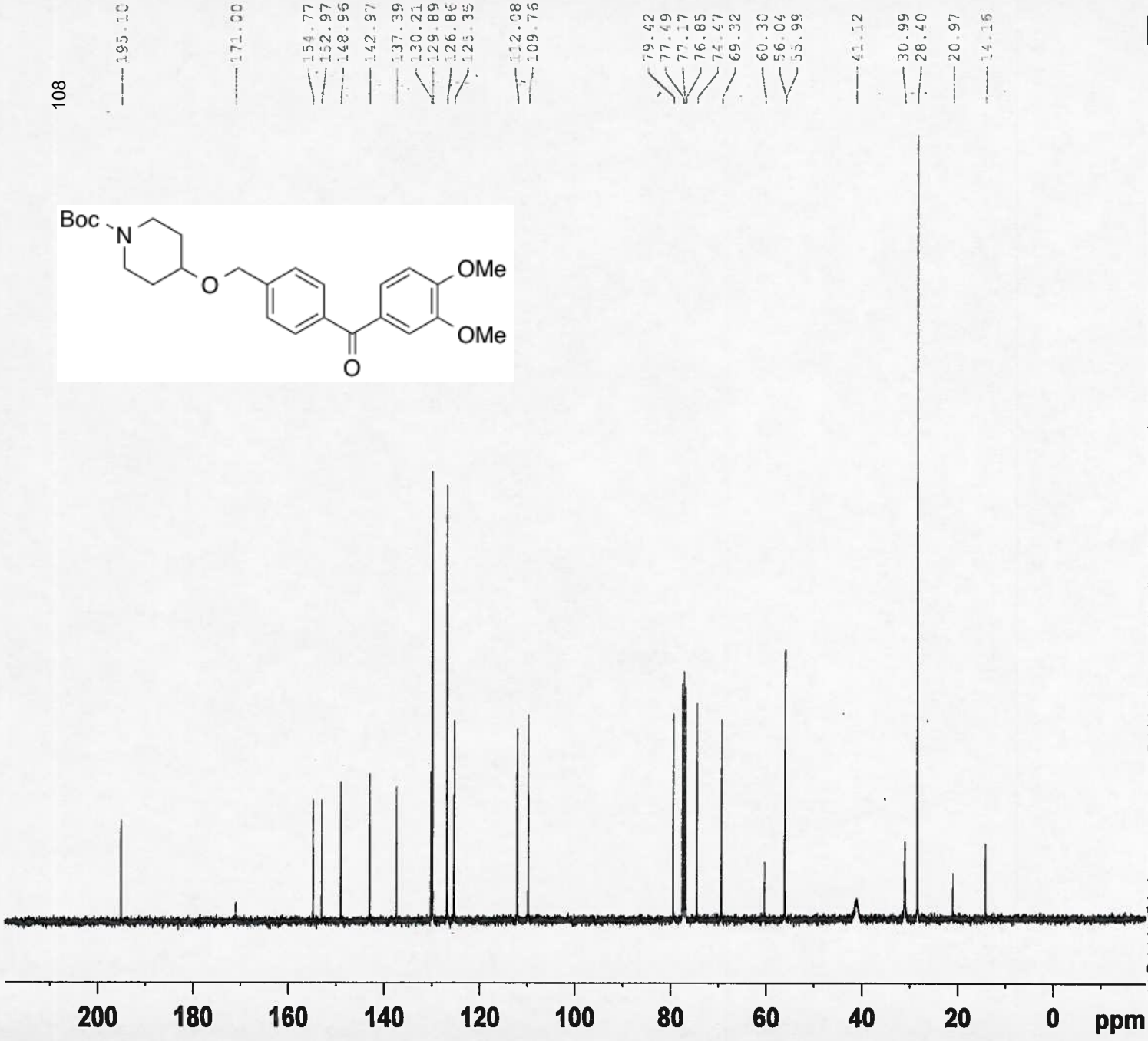
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400079 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDIII-47c-13C



BRUKER

Current Data Parameters

NAME	ZDIII-47c-13C
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140515
Time	18.18
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	81
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	181
DW	20.800 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

SFO1	100.6253441 MHz
NUC1	13C
P1	9.00 usec
PLW1	62.00000000 W

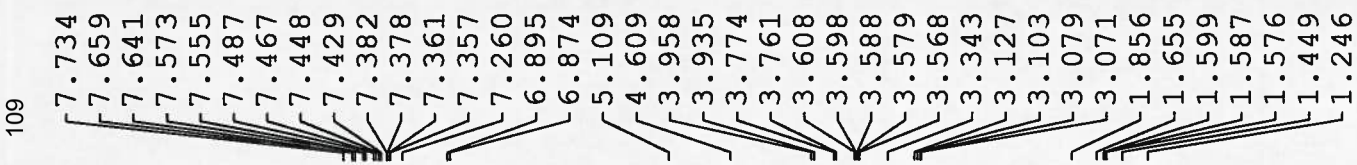
======== CHANNEL f2 ========

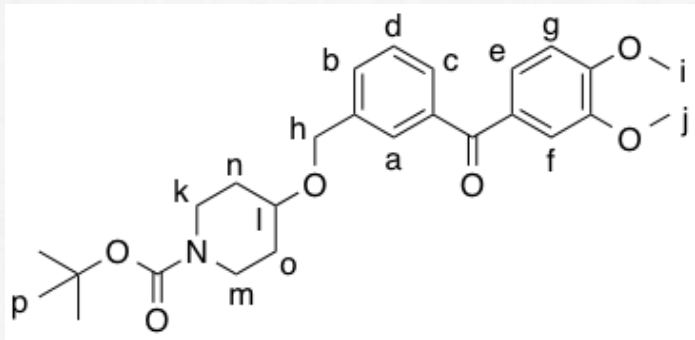
SFO2	400.1416006 MHz
NUC2	1H
CPDPRG[2	waltz16
PCPD2	90.00 usec
PLW2	16.00000000 W
PLW12	0.36000001 W
PLW13	0.29159999 W

F2 - Processing parameters

SI	32768
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

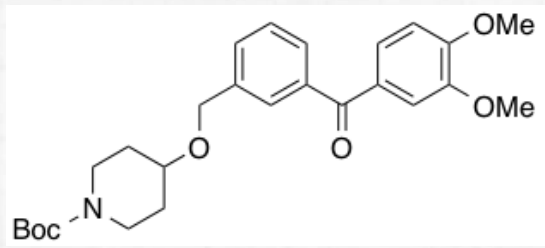
ZDII-73d





BRUKER

```
Current Data Parameters
NAME                  ZDII-73d
EXPNO                        3
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20140115
Time                     17.38
INSTRUM                  spect
PROBHD    5 mm PABBO BB-
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                          16
DS                           2
SWH                   8012.820 Hz
FIDRES                0.122266 Hz
AQ                    4.0894465 sec
RG                         101
DW                      62.400 usec
DE                       6.50 usec
TE                      298.0 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1                400.1424710 MHz
NUC1                        1H
P1                       13.50 usec
PLW1                16.00000000 W

F2 - Processing parameters
SI                      65536
SF                  400.1400082 MHz
WDW                        EM
SSB                  0
LB                       0.30 Hz
GB                   0
PC                       1.00
```



195.46
154.84
153.09
149.03
139.06
138.44
130.87
130.16
128.98
128.58
128.22
125.51
112.14
109.75
79.50
77.37
77.05
76.73
74.45
69.48
56.11
56.06
31.03
28.44

200 180 160 140 120 100 80 60 40 20 0 ppm

BRUKER

Current Data Parameters
NAME ZDII-73d-13C
EXPNO 2
PROCNO 1

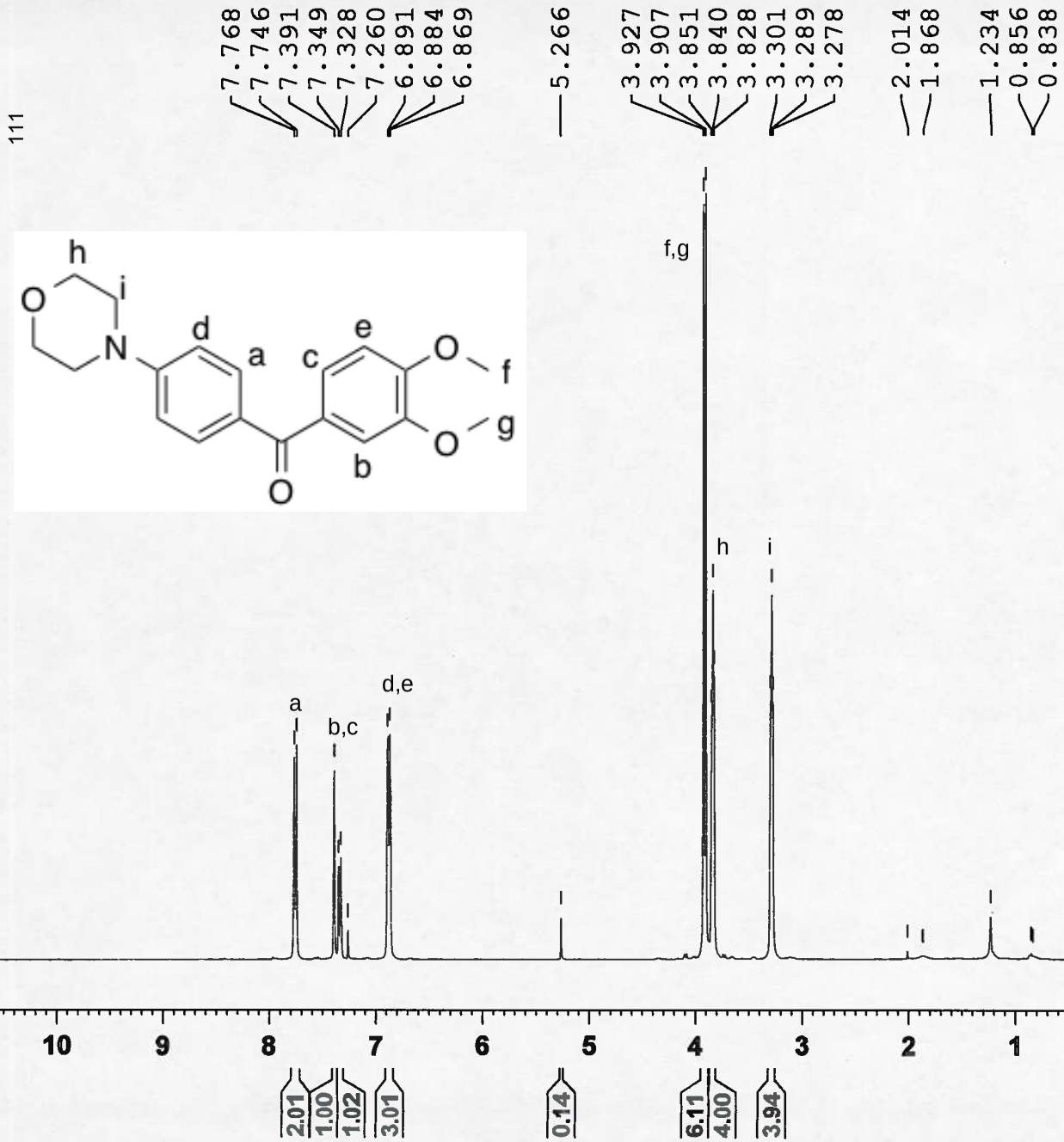
F2 - Acquisition Parameters
Date_ 20140114
Time 11.26
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 83
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 144
DW 20.800 usec
DE 6.50 usec
TE 298.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDII-75d



Current Data Parameters

NAME	ZDII-75d
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20140113
Time	17.21
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	32
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

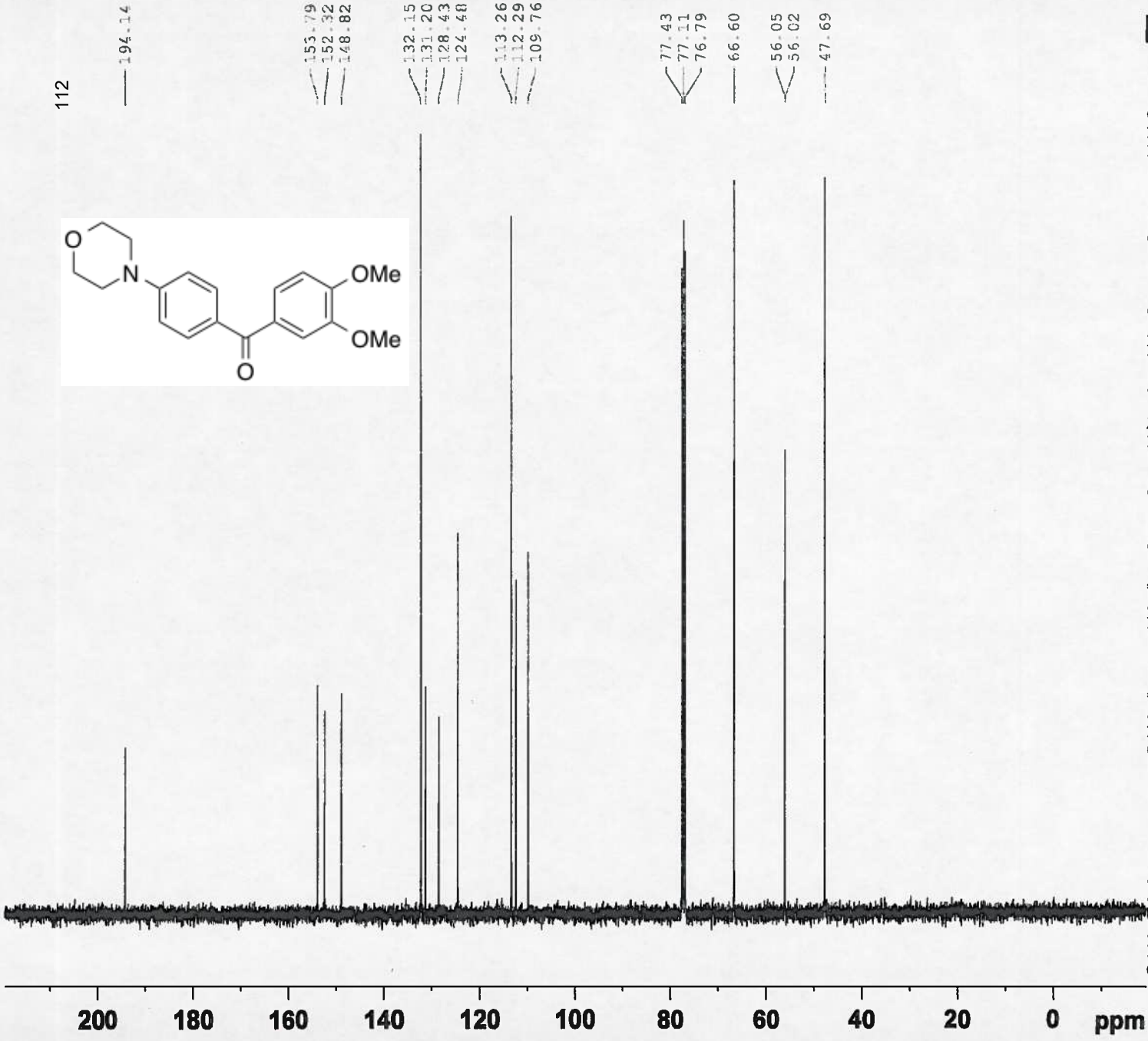
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400077 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

ZDII-75d-13C



BRUKER

Current Data Parameters
NAME ZDII-75d-13C
EXPNO 2
PROCNO 1

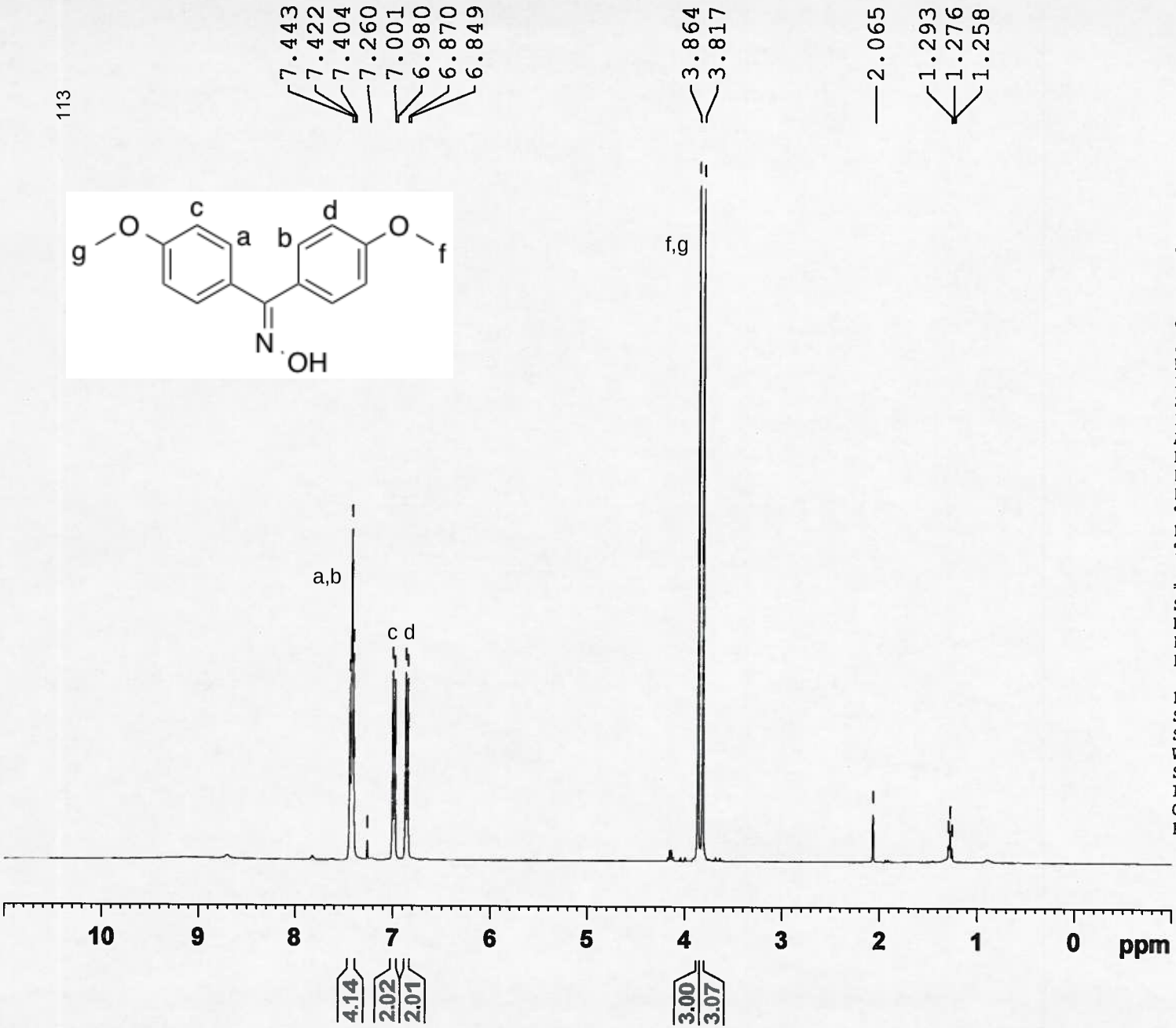
F2 - Acquisition Parameters
Date_ 20140113
Time 17.29
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 69
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 128
DW 20.800 usec
DE 6.50 usec
TE 298.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDII-105a



BRUKER

Current Data Parameters

NAME	ZDII-105a
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20140225
Time	10.22
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	50.8
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

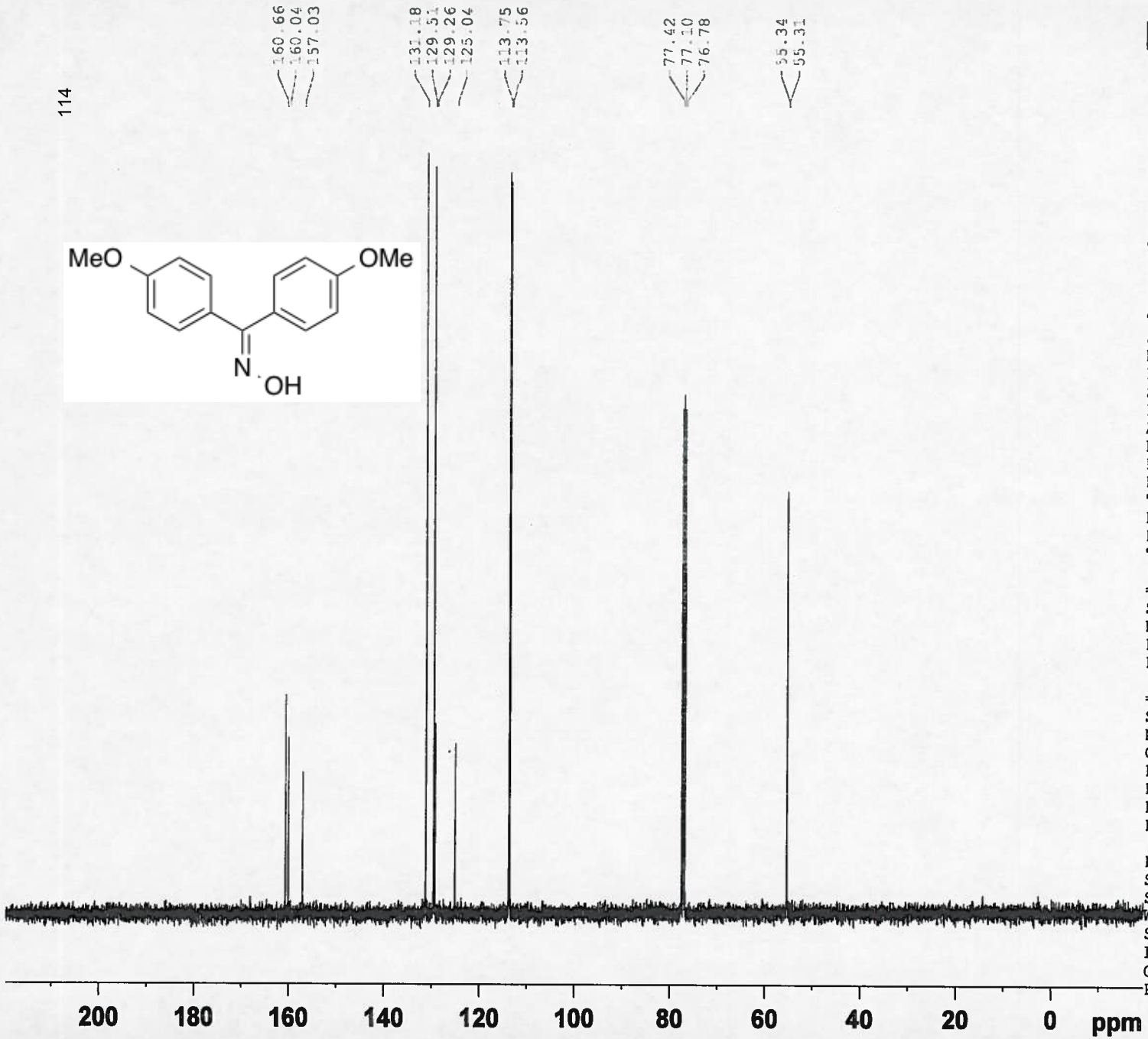
======== CHANNEL f1 ========

SFO1	400.1424710 MHz
NUC1	1H
P1	13.50 usec
PLW1	16.00000000 W

F2 - Processing parameters

SI	65536
SF	400.1400085 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

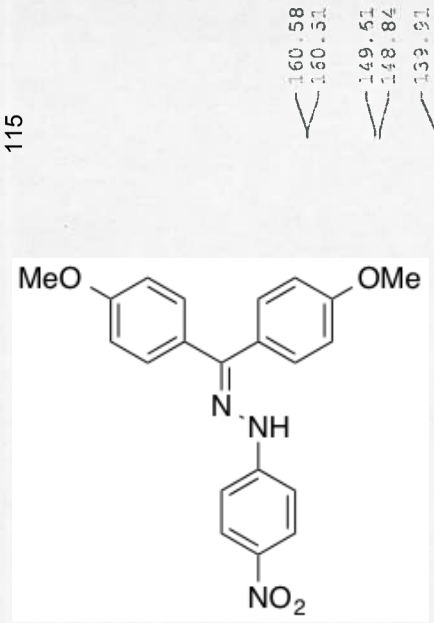
ZDII-105a-13C



BRUKER

```
Current Data Parameters
NAME       ZDII-105a-13C
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20140225
Time              10.27
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                   29
DS                    4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631488 sec
RG                  114
DW               20.800 usec
DE                6.50 usec
TE                298.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        100.6253441 MHz
NUC1                13C
P1                9.00 usec
PLW1        62.00000000 W

======== CHANNEL f2 ========
SFO2        400.1416006 MHz
NUC2                1H
CPDPRG[2        waltz16
PCPD2            90.00 usec
PLW2        16.00000000 W
PLW12        0.36000001 W
PLW13        0.29159999 W

F2 - Processing parameters
SI                 32768
SF          100.6152830 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

ZDII-119c-13C



160.58
150.51
149.51
148.84
139.91
132.23
130.50
130.32
128.62
126.14
123.82
115.20
113.77
113.47
111.77
77.36
77.04
76.73
55.44
55.38

115

200 180 160 140 120 100 80 60 40 20 0 ppm

BRUKER

Current Data Parameters
NAME ZDII-119c-13C
EXPNO 2
PROCNO 1

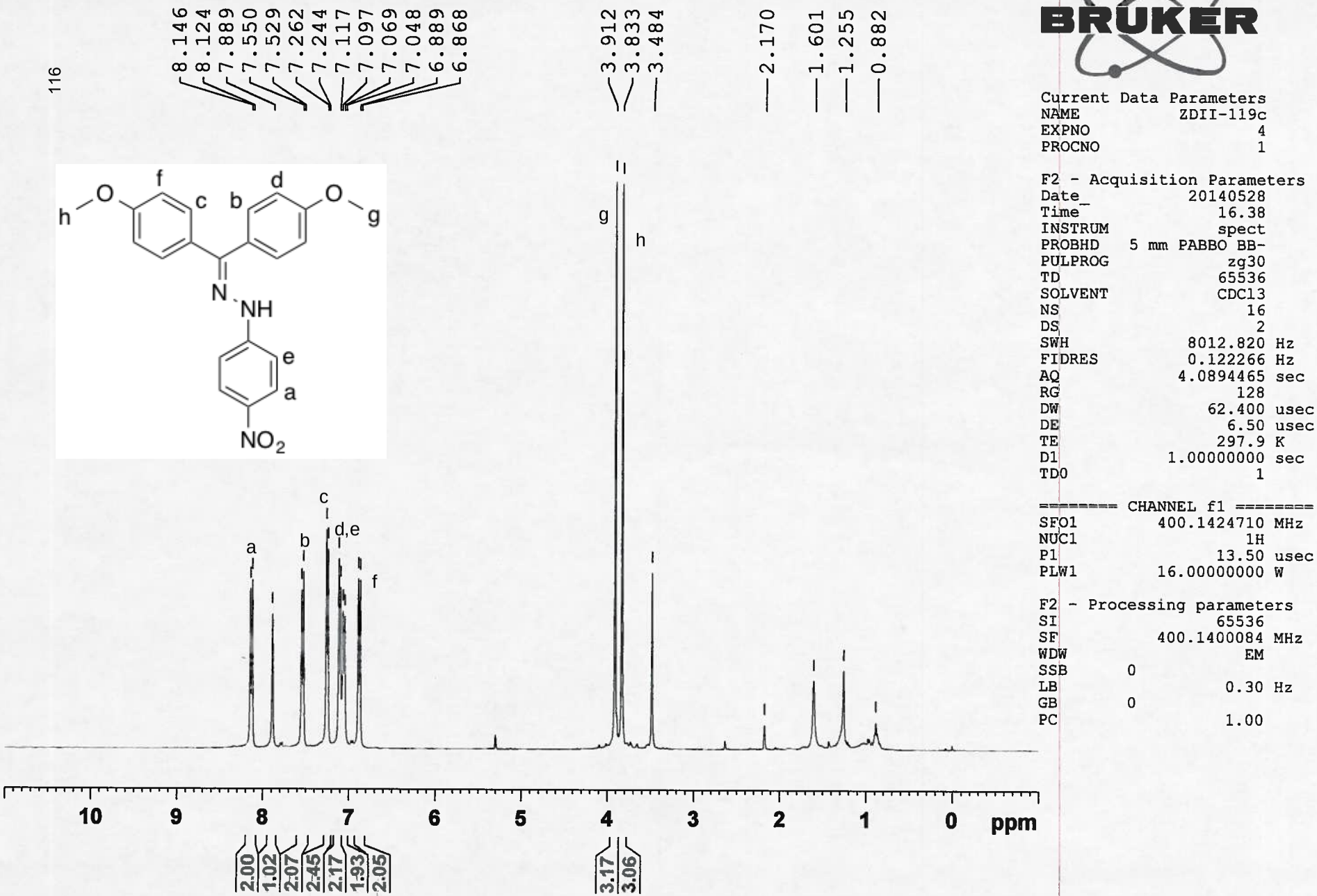
F2 - Acquisition Parameters
Date_ 20140303
Time 14.28
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 43
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 298.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 100.6253441 MHz
NUC1 13C
P1 9.00 usec
PLW1 62.00000000 W

======== CHANNEL f2 ========
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 16.00000000 W
PLW12 0.36000001 W
PLW13 0.29159999 W

F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ZDII-119c



BRUKER

Current Data Parameters
NAME ZDII-119c
EXPNO 4
PROCNO 1

F2 - Acquisition Parameters
Date_ 20140528
Time 16.38
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 128
DW 62.400 usec
DE 6.50 usec
TE 297.9 K
D1 1.00000000 sec
TD0 1

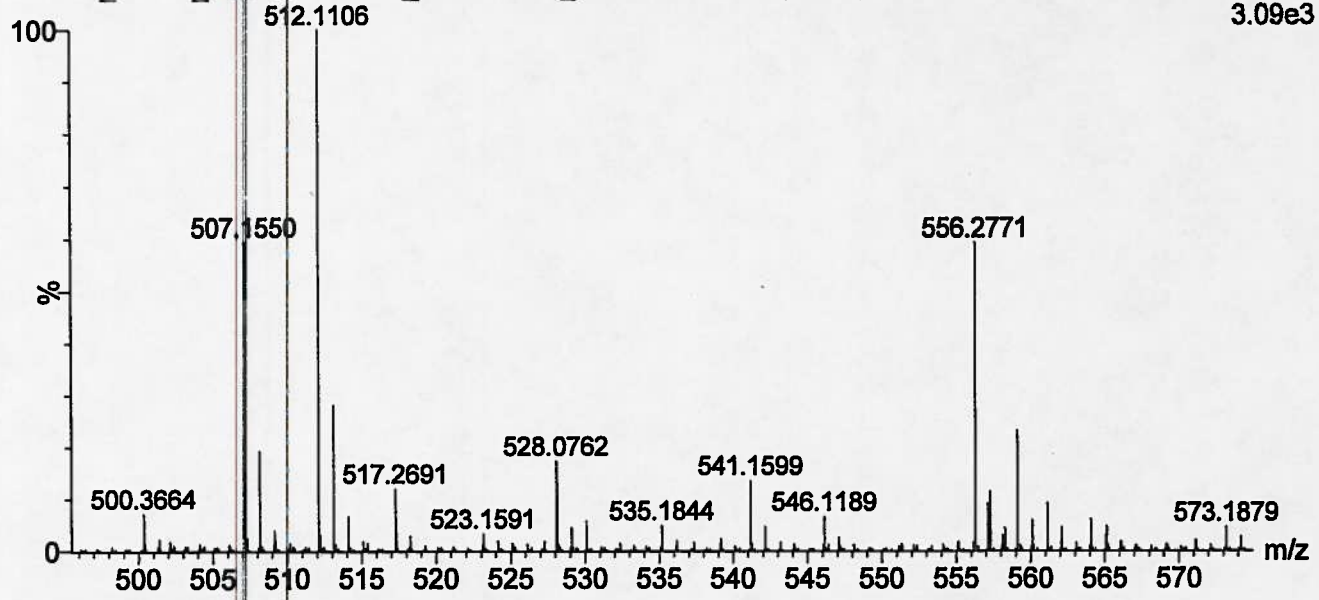
======== CHANNEL f1 ========
SFO1 400.1424710 MHz
NUC1 1H
P1 13.50 usec
PLW1 16.00000000 W

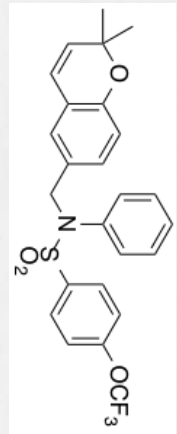
F2 - Processing parameters
SI 65536
SF 400.1400084 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

100%MeOH+0.1%HCOOH **13:53:44 31-Aug-2012**

SARAH_ZD-33_BWANG-ACCU_08-31-2012_ESI-POS01 119 (1.256) AM (Cen,2, 80.00, Ar,5000.0,556.28

3.09e3





Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
29508 formula(e) evaluated with 118 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 1-200 H: 1-200 N: 1-15 O: 1-100 F: 1-6 S: 1-50 Na: 1-2

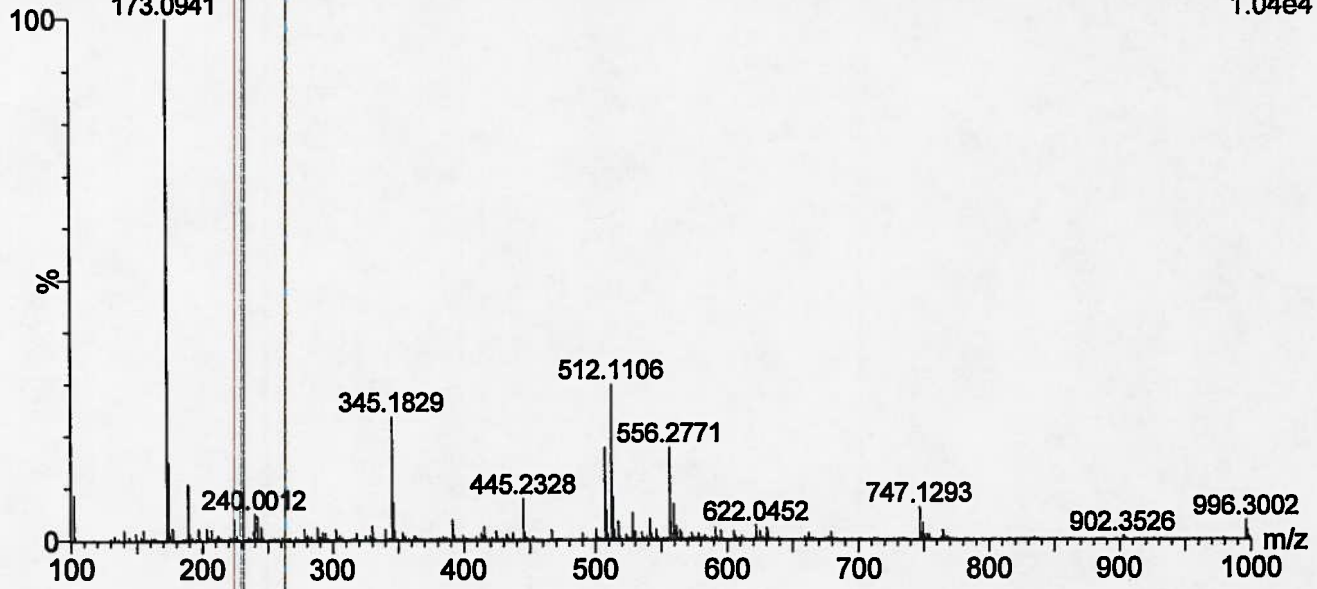
Minimum: -1.5

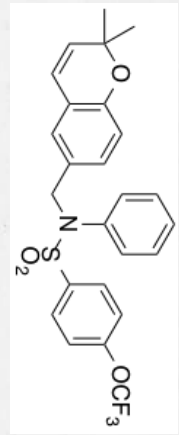
Maximum:		5.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
512.1106	512.1119	-1.3	-2.5	13.5	16.4	C25 H22 N O4 F3 S Na

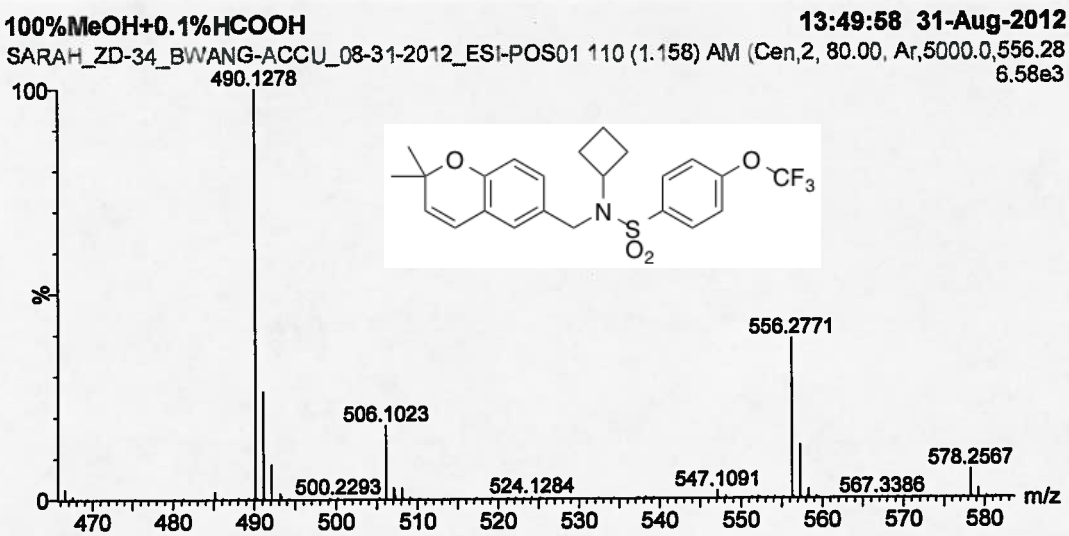
100%MeOH+0.1%HCOOH **13:53:44 31-Aug-2012**

SARAH_ZD-33_BWANG-ACCU_08-31-2012_ESI-POS01 119 (1.256) AM (Cen,2, 80.00, Ar,5000.0,556.28

1.04e4







Elemental Composition Report

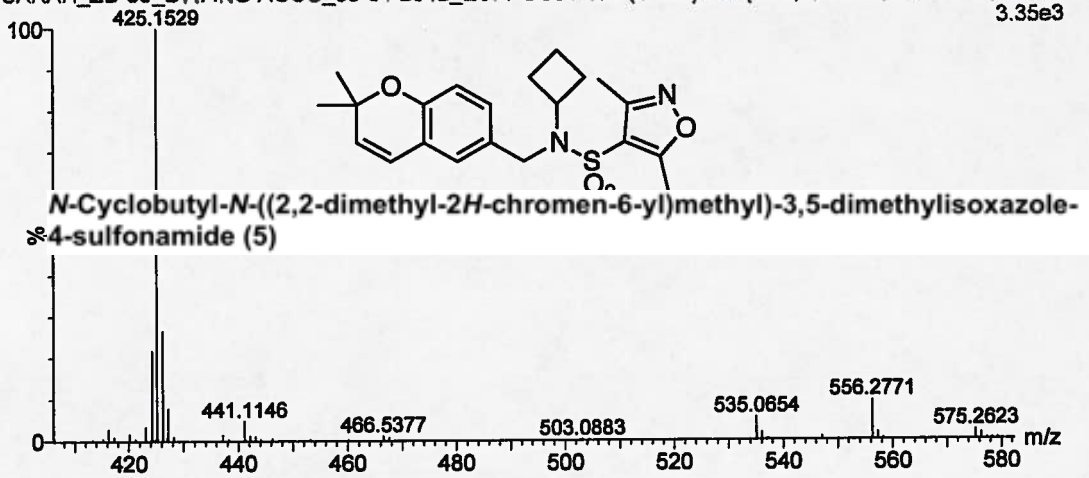
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
24118 formula(e) evaluated with 80 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 1-200 H: 1-200 N: 1-15 O: 1-100 F: 1-6 S: 1-50 Na: 1-2

Minimum:				-1.5		
Maximum:		5.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
490.1278	490.1276	0.2	0.4	10.5	1.0	C23 H24 N O4 F3 S Na

100%MeOH+0.1%HCOOH 13:36:08 31-Aug-2012

SARAH_ZD-35_BWANG-ACCU_08-31-2012_ESI-POS01 139 (1.475) AM (Cen,2, 80.00, Ar,5000.0,556.28 3.35e3



N-Cyclobutyl-*N*-((2,2-dimethyl-2*H*-chromen-6-yl)methyl)-3,5-dimethylisoxazole-4-sulfonamide (5)

Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

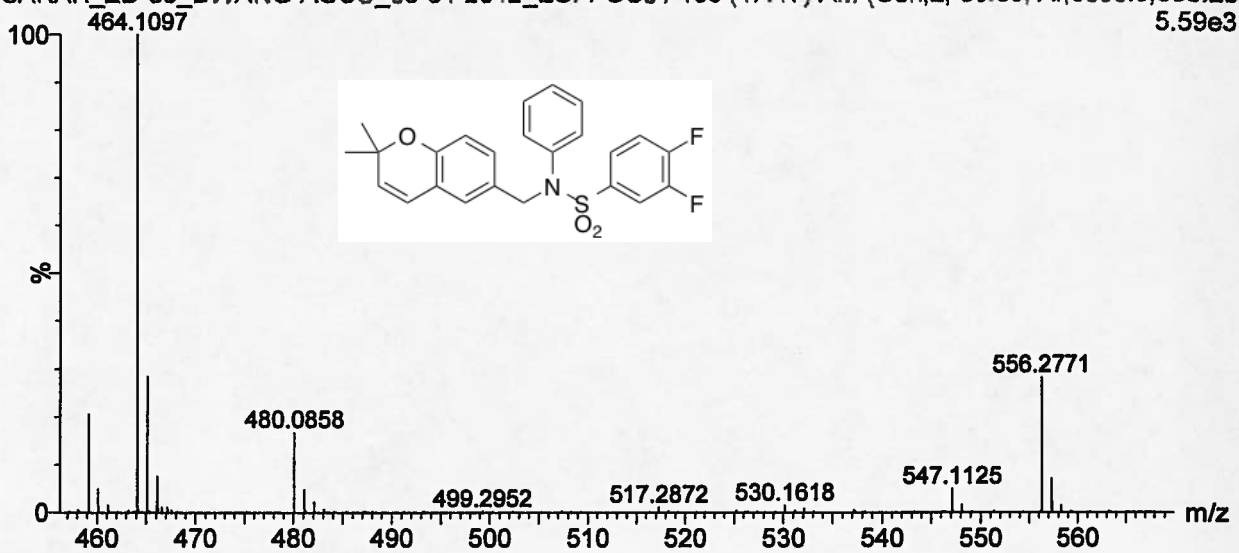
Monoisotopic Mass, Odd and Even Electron Ions
4305 formula(e) evaluated with 20 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 1-200 H: 1-200 N: 1-15 O: 1-100 S: 1-50 Na: 1-2

Minimum:				-1.5							
Maximum:		5.0		5.0	50.0						
Mass	Calc. Mass	mDa		PPM	DBE	i-FIT	Formula				
425.1529	425.1511	1.8		4.2	9.5	1.4	C21	H26	N2	O4	S
Na											

100%MeOH+0.1%HCOOH **13:45:26 31-Aug-2012**

SARAH_ZD-38_BWANG-ACCU_08-31-2012_ESI-POS01 135 (1.417) AM (Cen,2, 80.00, Ar,5000.0,556.28

5.59e3



Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

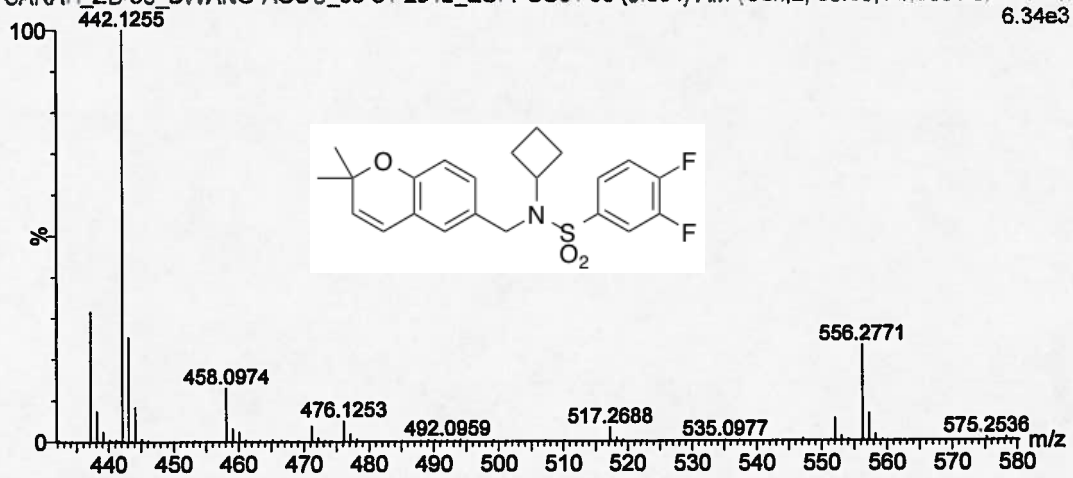
Monoisotopic Mass, Even Electron Ions
18747 formula(e) evaluated with 66 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 1-200 H: 1-200 N: 1-15 O: 1-100 F: 1-6 S: 1-50 Na: 1-2

Minimum:			-1.5			
Maximum:		5.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
464.1097	464.1108	-1.1	-2.4	13.5	5.7	C24 H21 N O3 F2 S Na

100%MeOH+0.1%HCOOH **13:41:23 31-Aug-2012**

SARAH_ZD-39_BWANG-ACCU_08-31-2012_ESI-POS01 66 (0.694) AM (Cen,2, 80.00, Ar,5000.0,556.28,(

6.34e3

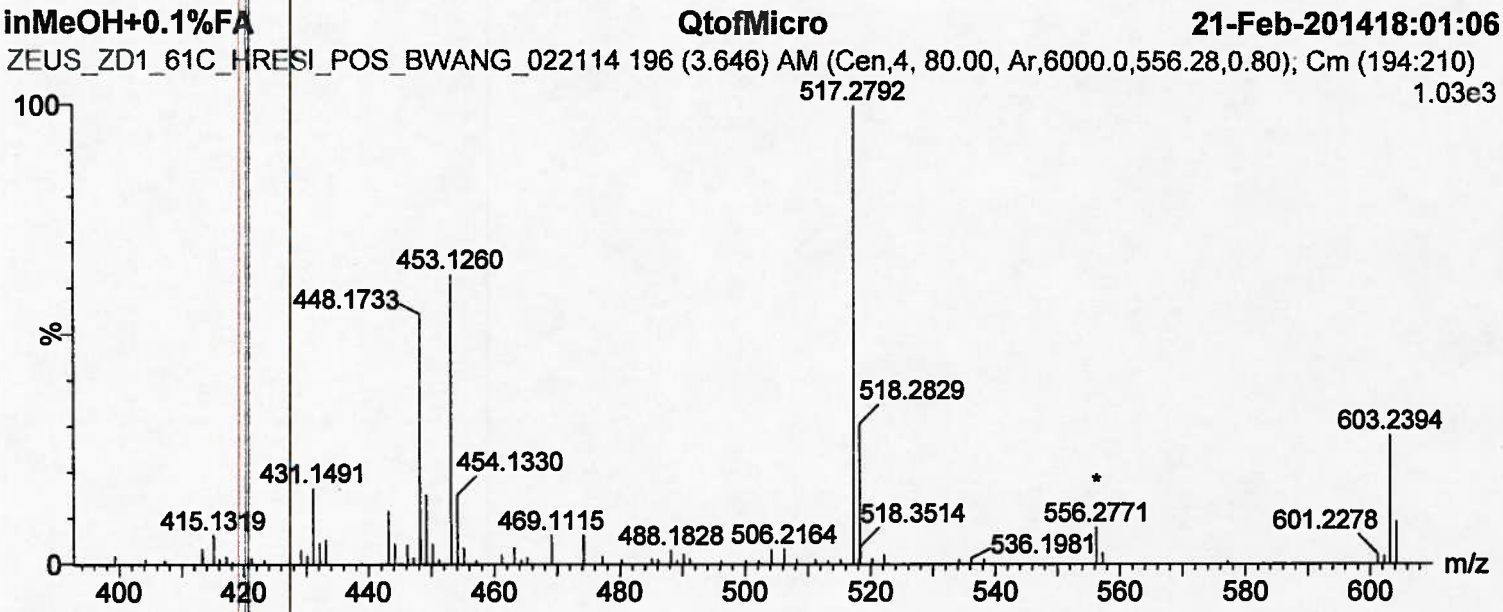


Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
14806 formula(e) evaluated with 47 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 1-200 H: 1-200 N: 1-15 O: 1-100 F: 1-6 S: 1-50 Na: 1-2

Minimum:			-1.5			
Maximum:		5.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
442.1255	442.1264	-0.9	-2.0	10.5	0.7	C22 H23 N O3 F2 S Na

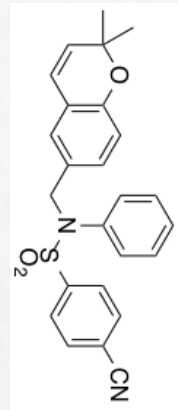


Elemental Composition Report

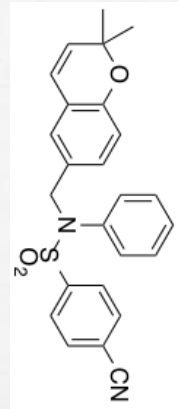
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1819 formula(e) evaluated with 15 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 5-80 H: 5-80 N: 1-10 O: 1-15 S: 1-2 23Na: 0-1

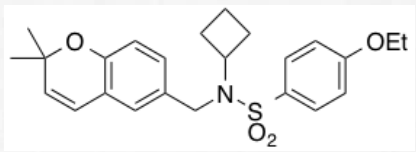
Minimum:			-1.5
Maximum:	800.0	5.0	200.0



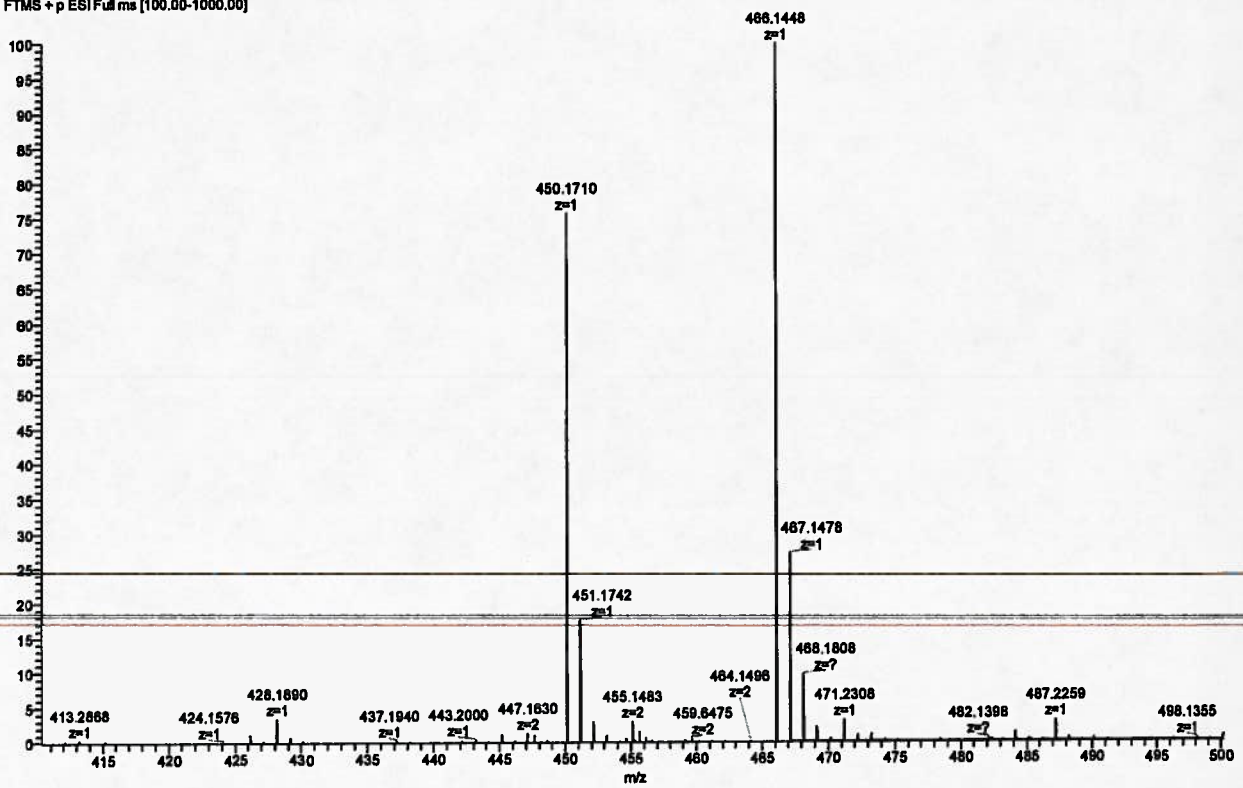
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
453.1260	453.1256	0.4	0.9	11.5	20.9	C18 H22 N8 O S2 23Na
	453.1265	-0.5	-1.1	6.5	7.9	C11 H21 N10 O8 S
	453.1266	-0.6	-1.3	9.5	25.3	C19 H25 N4 O5 S2
	453.1267	-0.7	-1.5	2.5	8.7	C13 H26 N4 O10 S 23Na
	453.1251	0.9	2.0	1.5	13.9	C10 H25 N6 O12 S
	453.1249	1.1	2.4	15.5	10.0	C25 H22 N2 O3 S 23Na
	453.1273	-1.3	-2.9	18.5	14.3	C27 H21 N2 O3 S
	453.1246	1.4	3.1	19.5	8.5	C23 H17 N8 O S
	453.1274	-1.4	-3.1	-1.5	35.5	C6 H26 N10 O8 S2 23Na
	453.1242	1.8	4.0	6.5	23.7	C17 H26 N4 O5 S2 23Na
	453.1240	2.0	4.4	3.5	11.5	C9 H22 N10 O8 S 23Na
	453.1280	-2.0	-4.4	14.5	23.7	C20 H21 N8 O S2
	453.1240	2.0	4.4	10.5	21.3	C15 H21 N10 O3 S2
	453.1281	-2.1	-4.6	7.5	4.6	C14 H22 N8 O6 S 23Na
	453.1283	-2.3	-5.1	10.5	26.3	C22 H26 N2 O3 S2 23Na



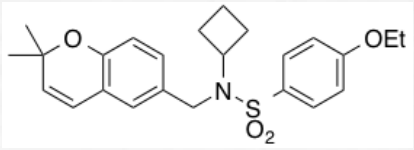
Zeus_ZDI-64c_BWang-ACCU_POS_01222014_01 #1-16 RT: 0.00-0.33 SB: 2 0.33 , 0.33 NL: 1.50E7
T: FTMS + p ESI Full ms [100.00-1000.00]



Zeus_ZDI-64c_BWang-ACCU_POS_01222014_01 #1-16 RT: 0.00-0.33 SB: 2 0.33 , 0.33 NL: 9.58E6
T: FTMS + p ESI Full ms [100.00-1000.00]



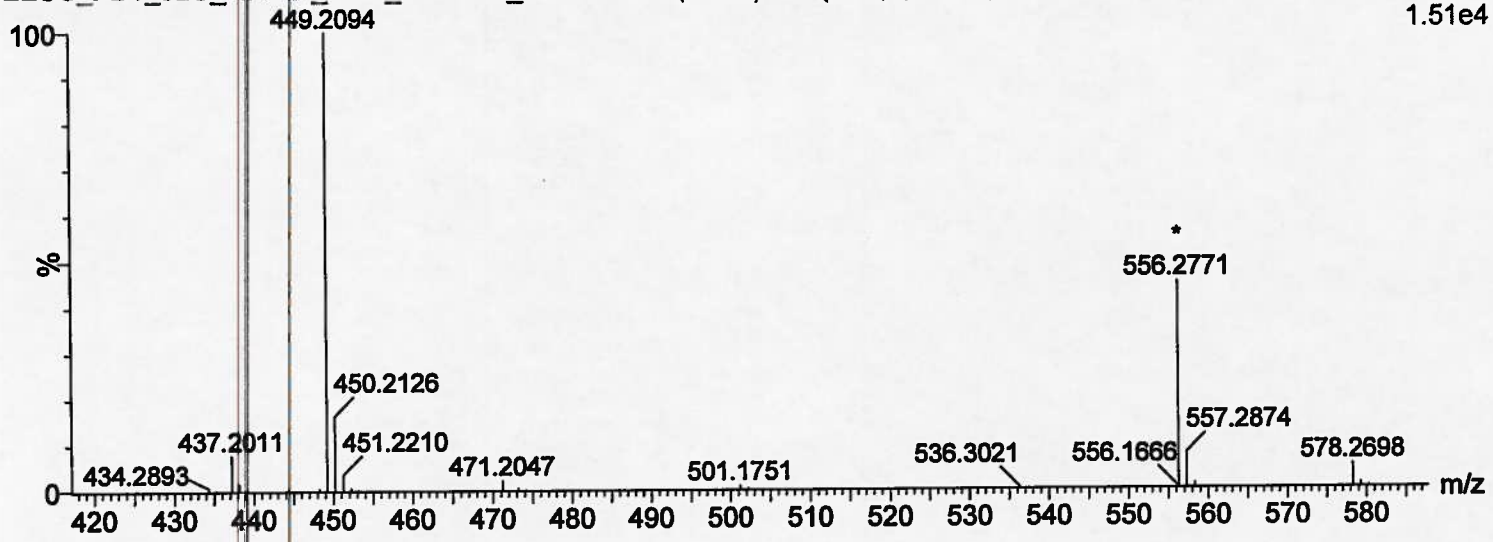
SPECTRUM - simulation :

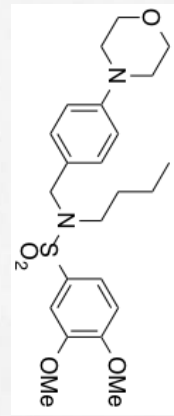


m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
450.1709	450.1710	-0.02	10.5	C24 H29 O4 N Na S

inMeOH+0.1%FA QtofMicro 21-Feb-201419:11:36

ZEUS_ZD1_82C_HRESI_POS_BWANG_022114 314 (5.833) AM (Cen,4, 80.00, Ar,6000.0,556.28,0.80); Cm (310:325)





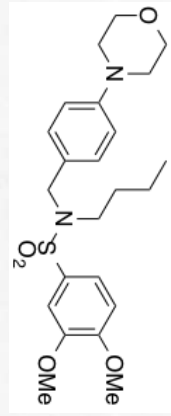
Elemental Composition Report

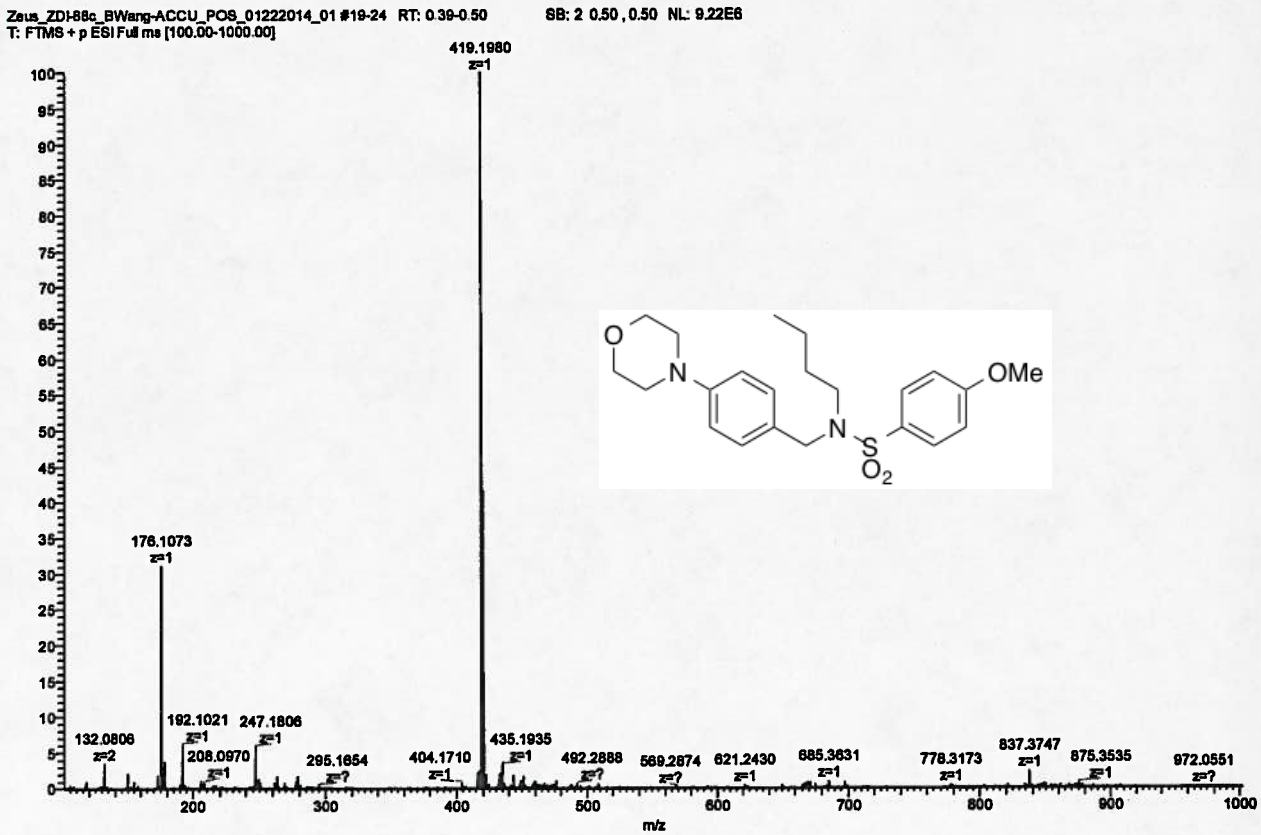
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

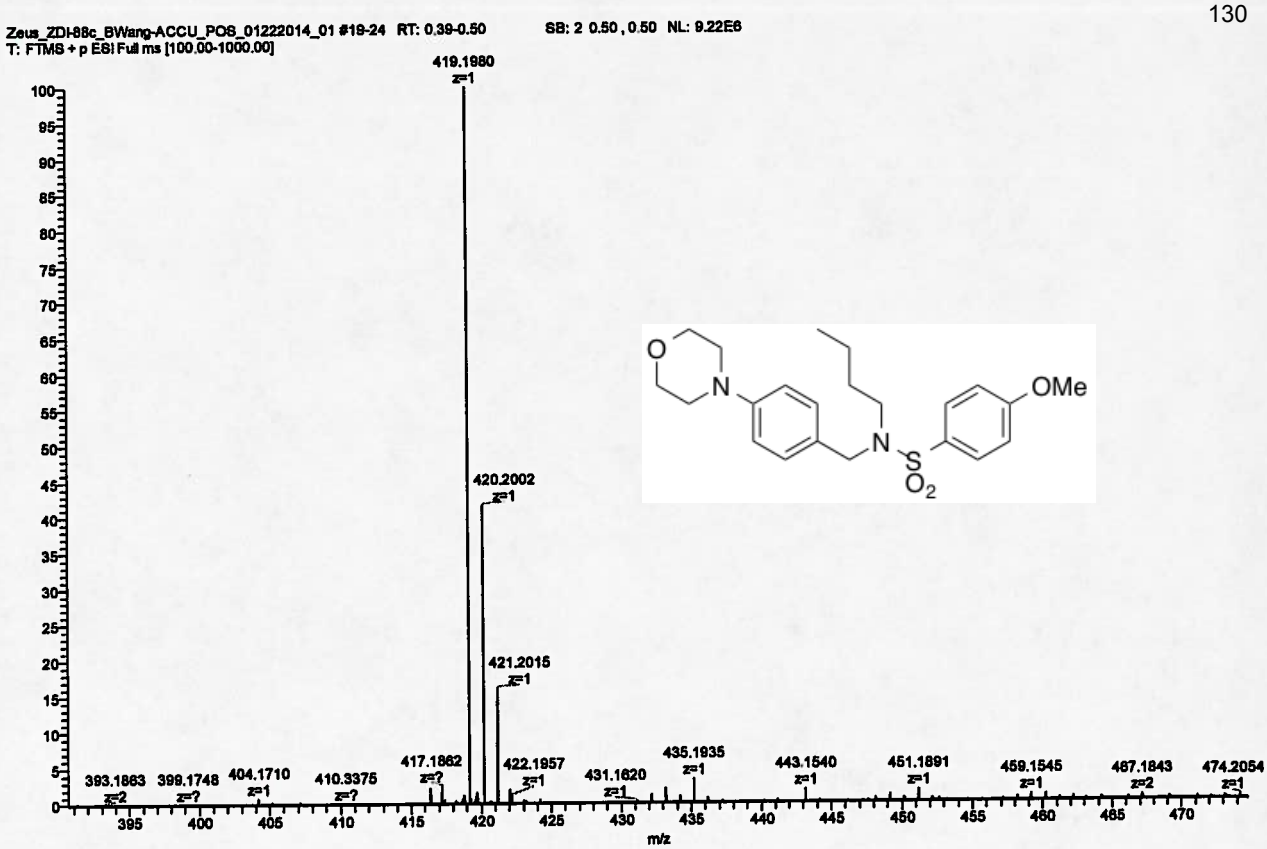
Monoisotopic Mass, Even Electron Ions
959 formula(e) evaluated with 4 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 5-80 H: 5-80 N: 1-10 O: 1-15 S: 1-2

Minimum:				-1.5		
Maximum:		800.0	5.0	200.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
449.2094	449.2104	-1.0	-2.2	-0.5	1253.7	C15 H37 N4 O7 S2

449.2083	1.1	2.4	9.5	595.9	C19 H29 N8 O3 S
449.2110	-1.6	-3.6	8.5	832.1	C23 H33 N2 O5 S
449.2077	1.7	3.8	0.5	1086.3	C11 H33 N10 O5 S2

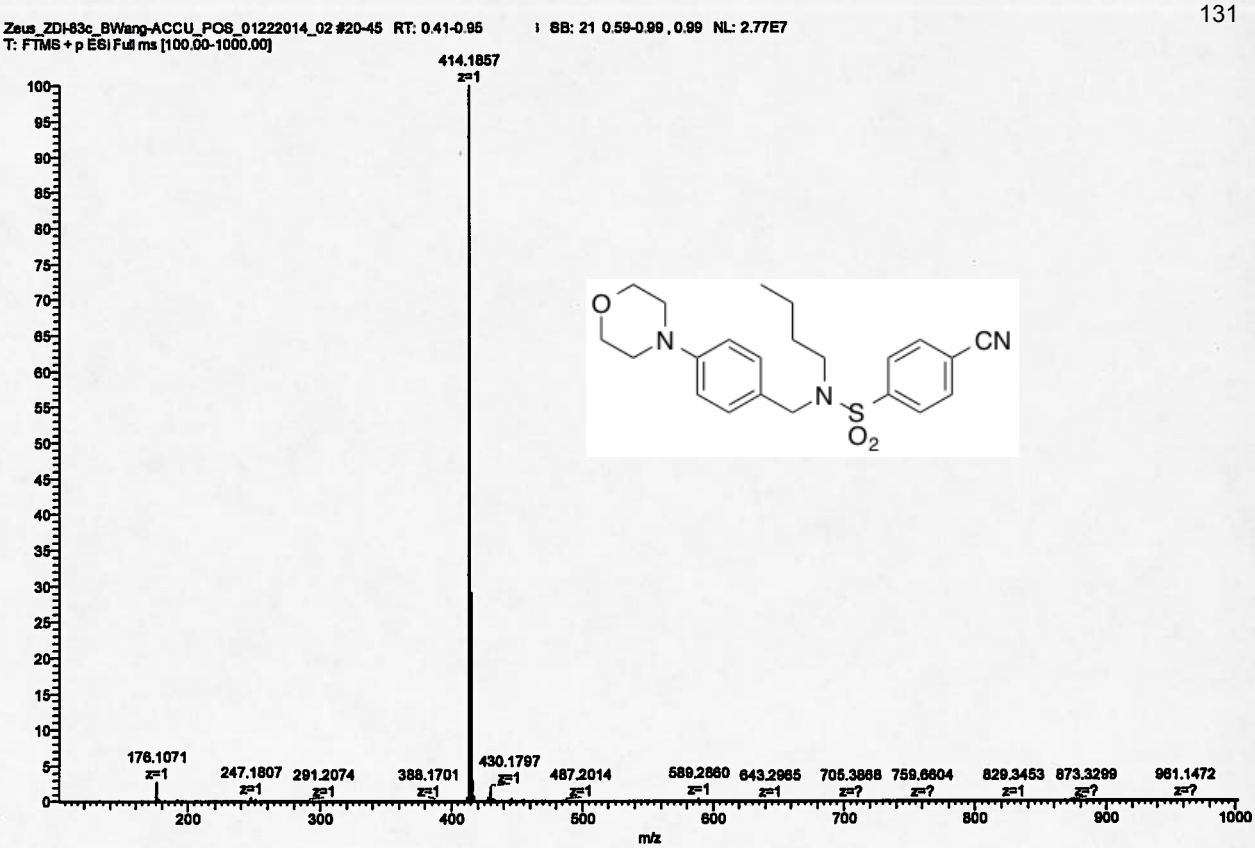


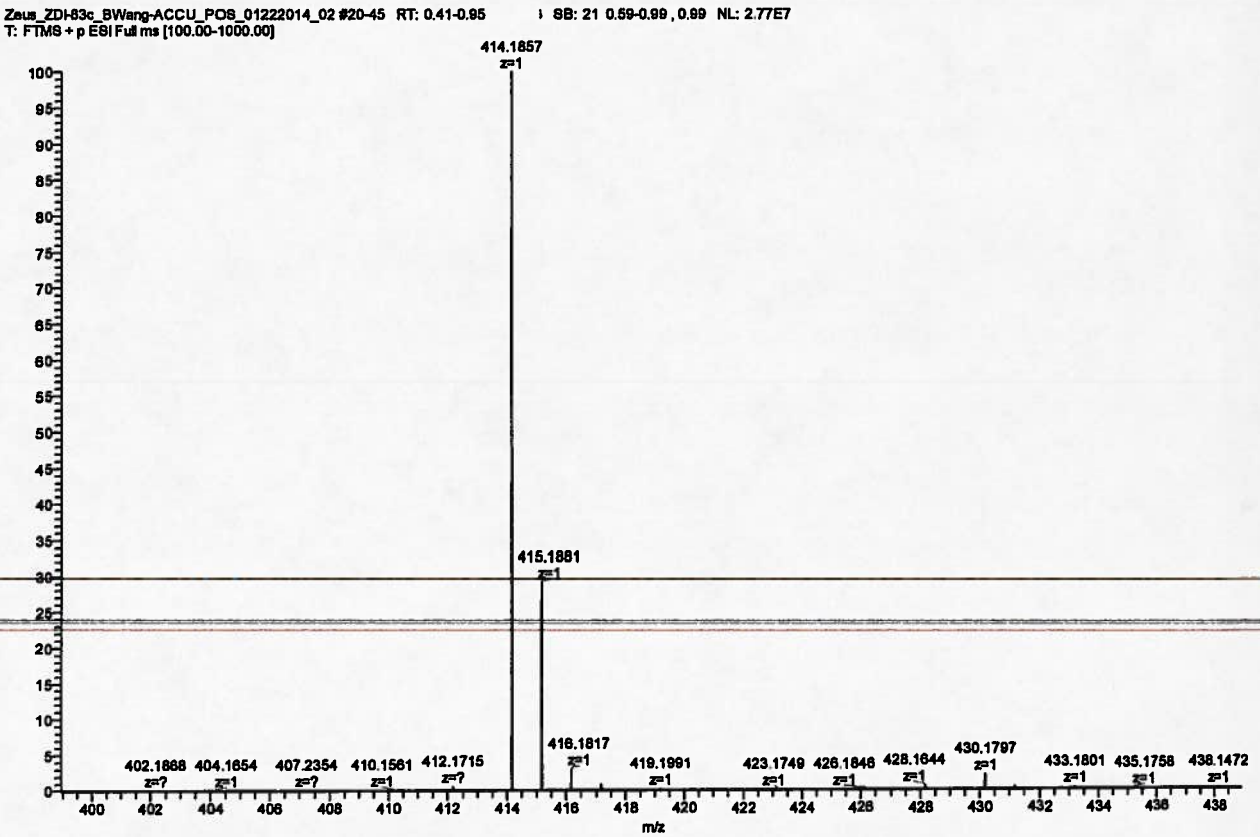

Zeus_ZDI-88c_BWang-ACCU_POS_01222014_01 #19-24 RT: 0.39-0.50 SB: 2 0.50 , 0.50 NL: 9.22E6
T: FTMS + p ESI Full ms [100.00-1000.00]
419.1980 z=1
176.1073 z=1
132.0806 z=2
192.1021 z=1
247.1806 z=1
208.0970 z=1
295.1654 z=?
404.1710 z=1
435.1935 z=1
492.2888 z=?
569.2874 z=?
621.2430 z=1
685.3631 z=1
778.3173 z=1
837.3747 z=1
875.3535 z=1
972.0551 z=?
m/z
O
N
N
S
O2
OMe



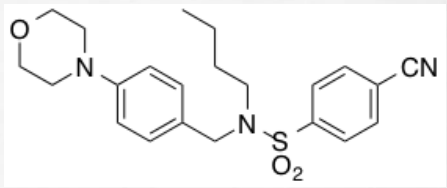
SPECTRUM - simulation :

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
419.1980	419.1999	-4.52	8.5	C22 H31 O4 N2 S


Zeus_ZDH-83c_BWang-ACCU_POS_01222014_02 #20-45 RT: 0.41-0.95 SB: 21 0.59-0.99 , 0.99 NL: 2.77E7
T: FTMS + p ESI Full ms [100.00-1000.00]
414.1857
z=1
176.1071
z=1
247.1807
z=1
291.2074
z=1
388.1701
z=1
430.1797
z=1
487.2014
z=1
589.2860
z=1
643.2965
z=1
705.3868
z=?
759.6604
z=?
829.3453
z=1
873.3299
z=?
961.1472
z=?
m/z
O
N
N
S
O2
CN

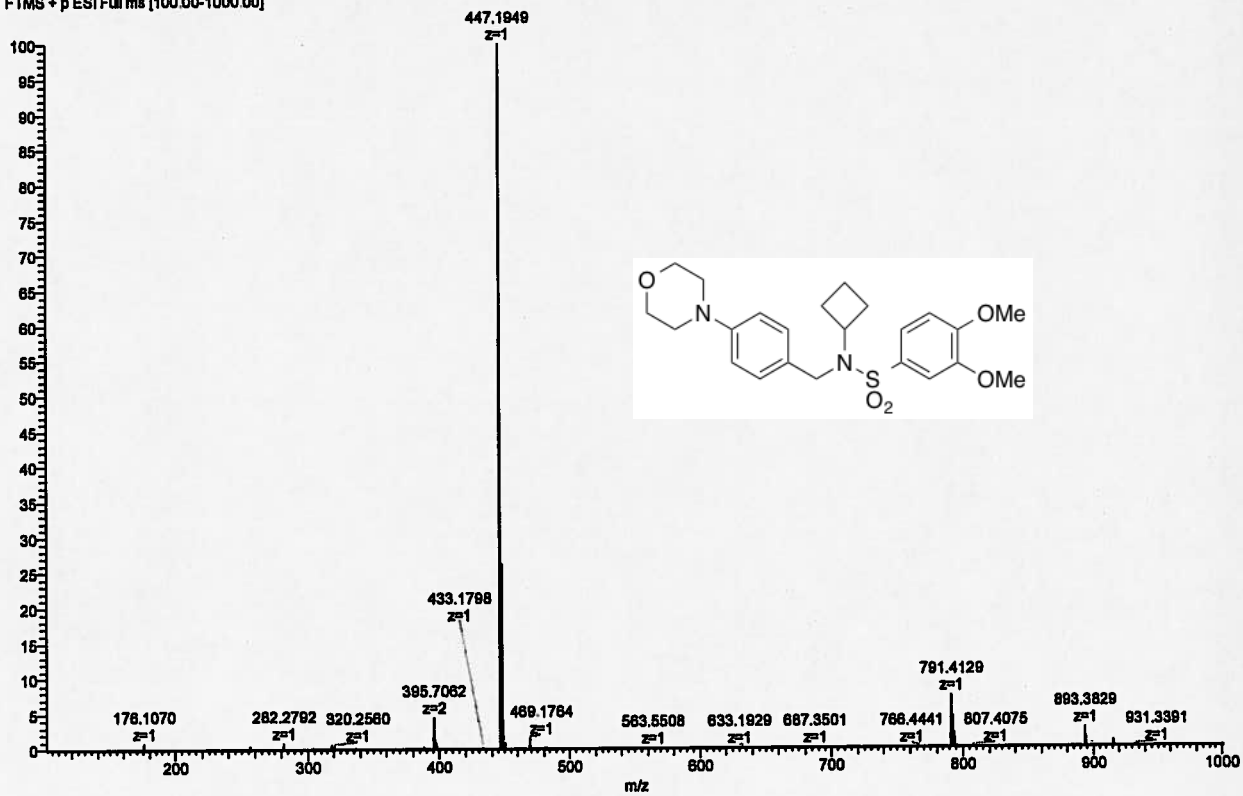

Zeus_ZDH-83c_BWang-ACCU_POS_01222014_02 #20-45 RT: 0.41-0.95 SB: 21 0.59-0.99 , 0.99 NL: 2.77E7
T: FTMS + p ESI Full ms [100.00-1000.00]
414.1857
z=1
415.1881
z=1
402.1868
z=?
404.1654
z=1
407.2354
z=?
410.1561
z=1
412.1715
z=?
416.1817
z=1
419.1991
z=1
423.1749
z=1
426.1848
z=1
428.1644
z=1
430.1797
z=1
433.1801
z=1
435.1758
z=1
438.1472
z=1
m/z

SPECTRUM - simulation :

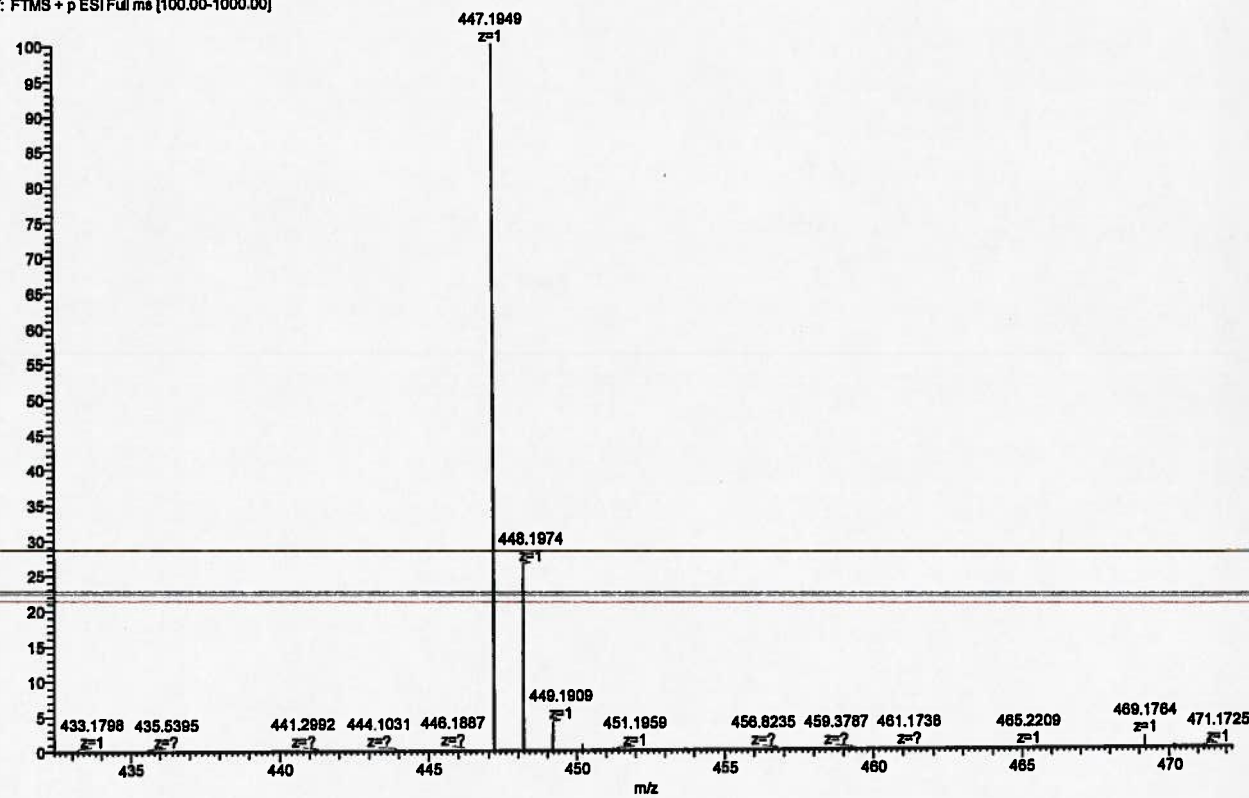


m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
414.1857	414.1846	2.71	10.5	C22 H28 O3 N3 S

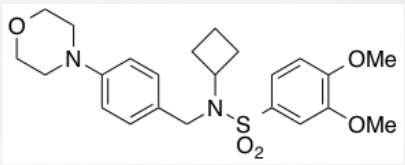
Zeus_ZDI_27d_BWang-Accu_12112013_ESI-POS-01 #185-193 RT: 2 AV: 9 SB: 89 0.58-1.41 , 2.72-3.09 NL: 8.25E8
T: FTMS + p ESI Full ms [100.00-1000.00]



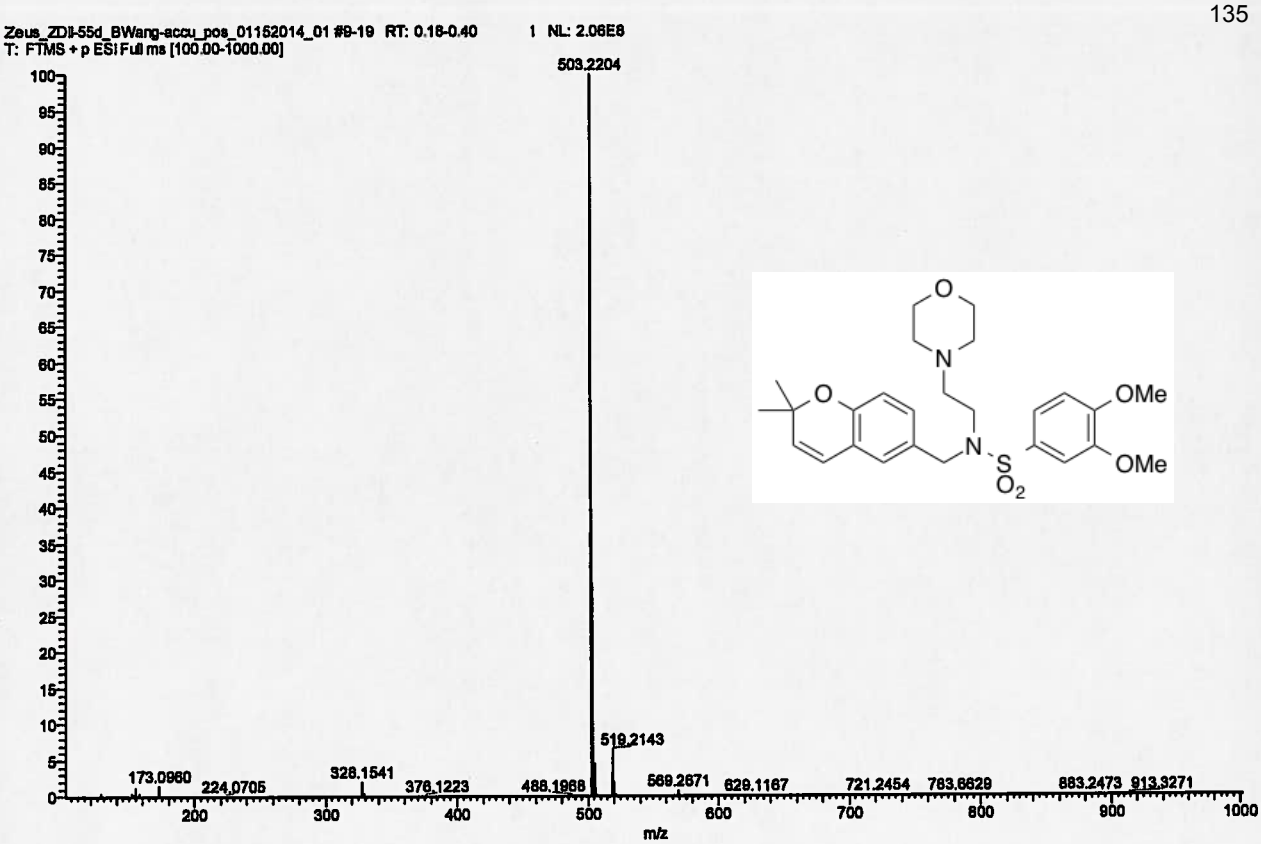
Zeus_ZDI_27d_BWang-Accu_12112013_ESI-POS-01 #185-193 RT: 2 AV: 9 SB: 89 0.58-1.41 , 2.72-3.09 NL: 8.25E8
T: FTMS + p ESI Full ms [100.00-1000.00]

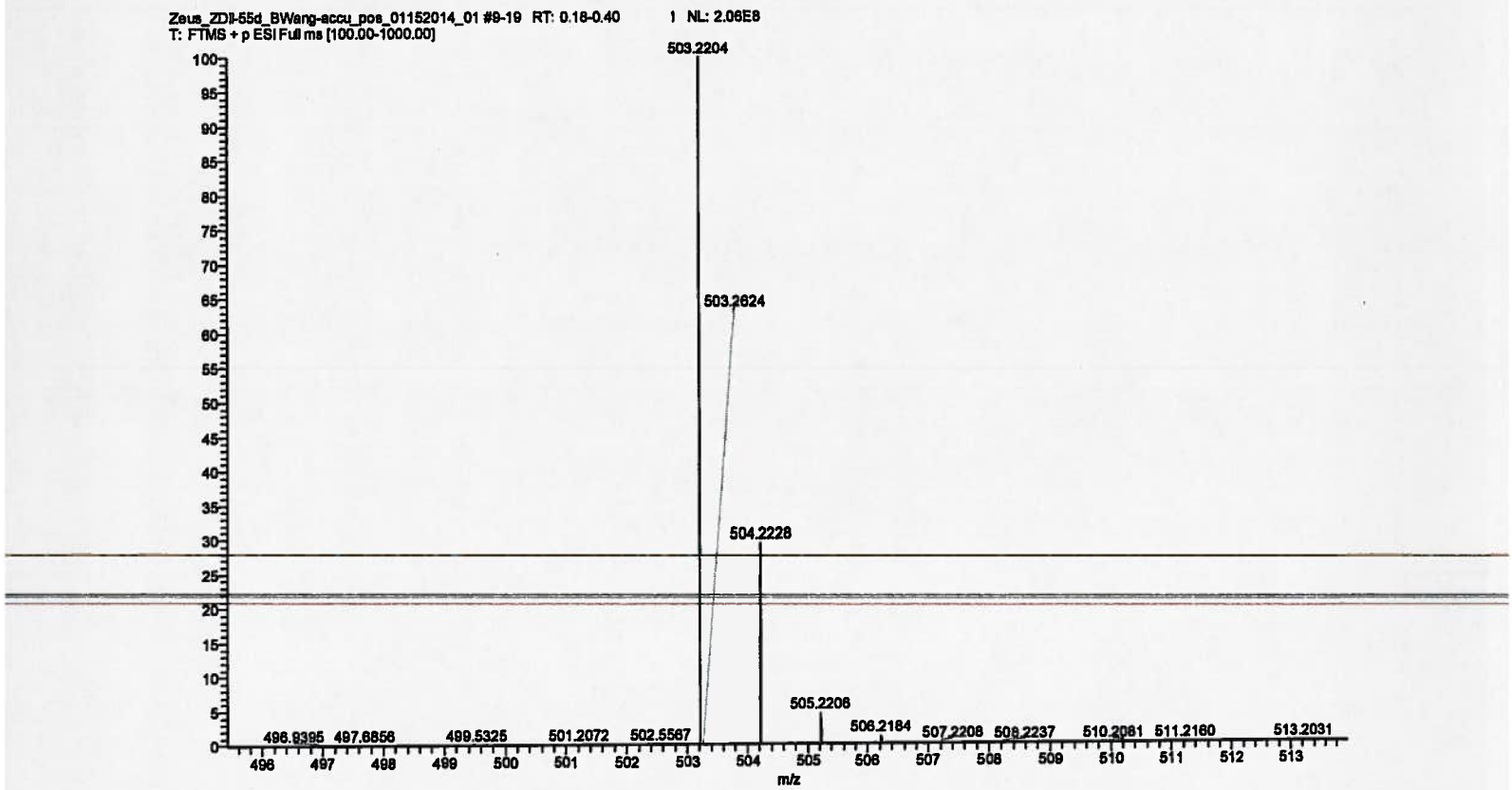


SPECTRUM - simulation :

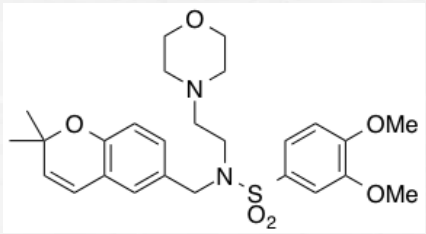


m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
447.1949	447.1948	0.18	9.5	C23 H31 O5 N2 S

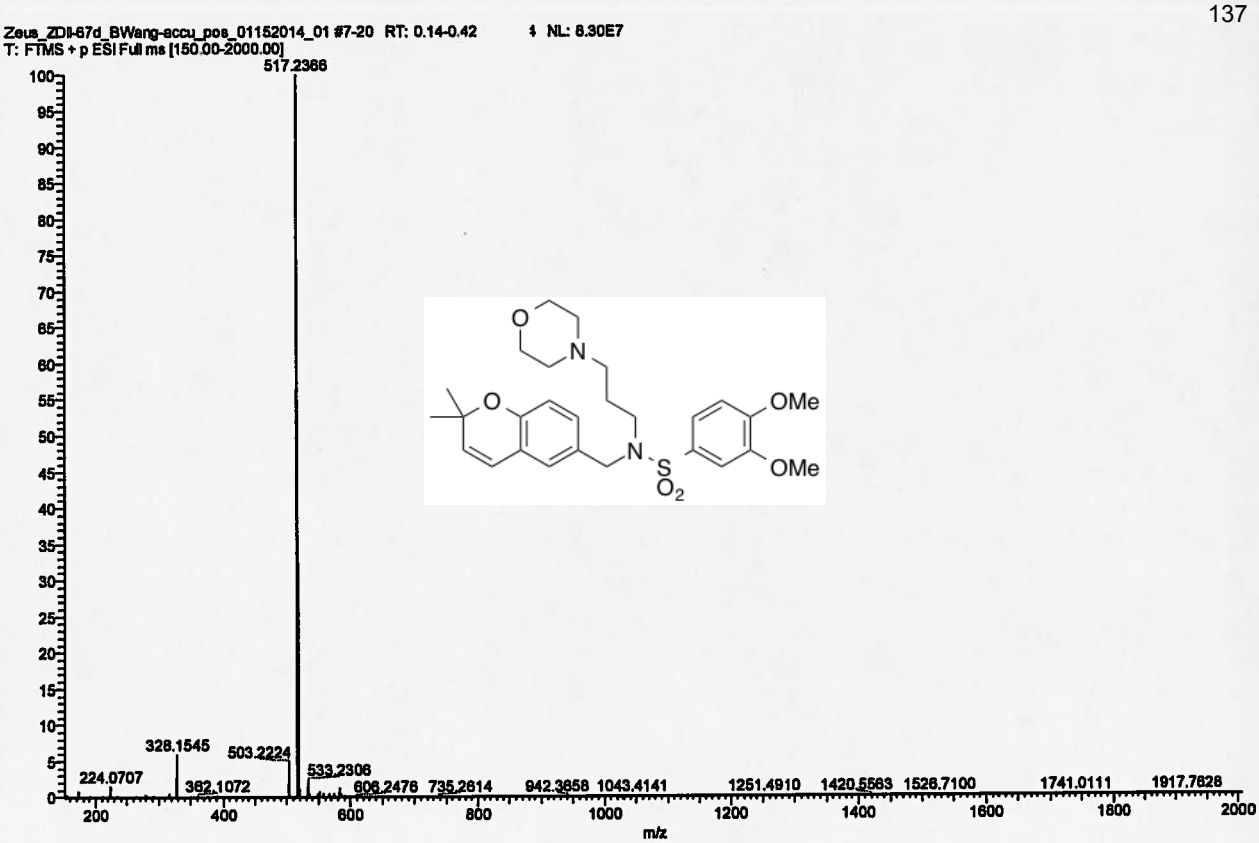

Zeus_ZDI-55d_BWang-accu_pos_01152014_01 #9-19 RT: 0.18-0.40 1 NL: 2.06E8
T: FTMS + p ESI Full ms [100.00-1000.00]
503.2204
519.2143
173.0960
224.0705
328.1541
376.1223
488.1968
569.2671
629.1167
721.2454
783.6629
883.2473
913.3271
m/z
O
N
O
N
S
O2
OMe
OMe

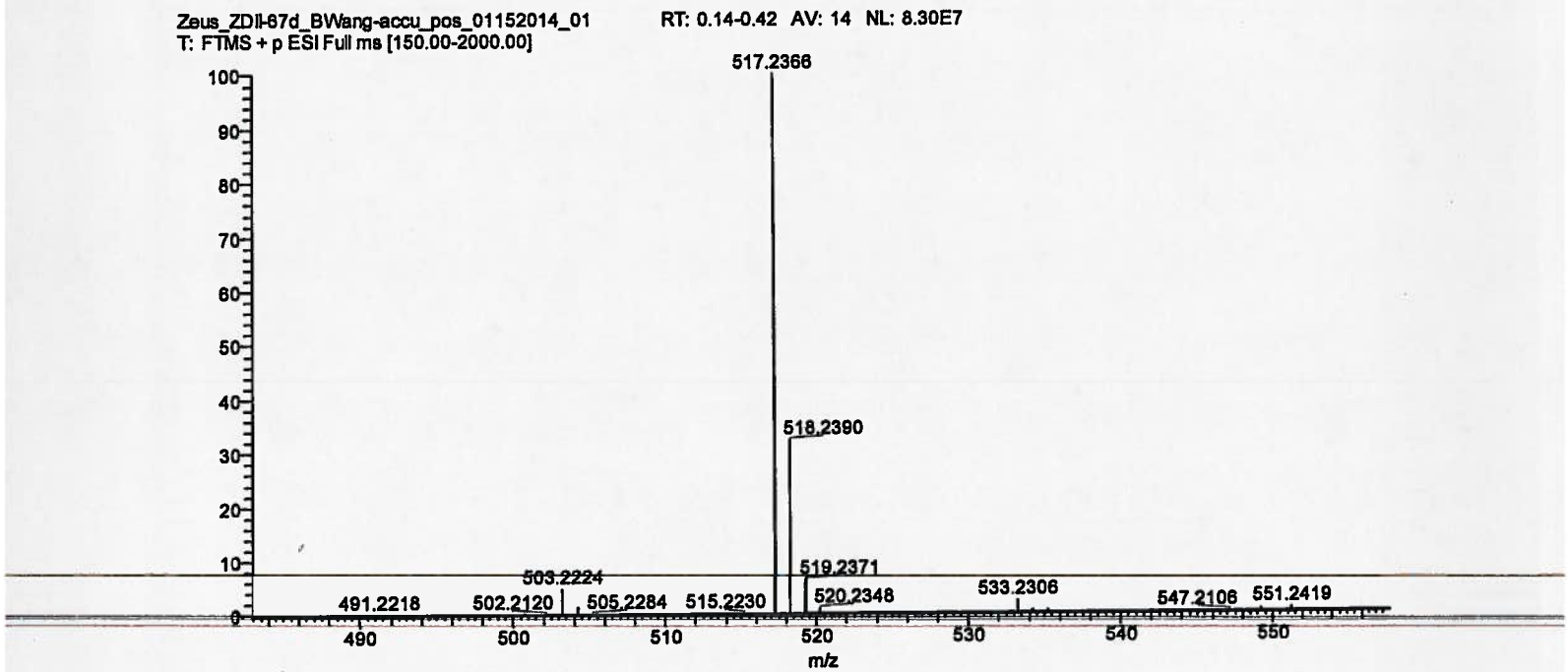

Zeus_ZDI-55d_BWang-accu_pos_01152014_01 #9-19 RT: 0.18-0.40 1 NL: 2.06E8
T: FTMS + p ESI Full ms [100.00-1000.00]
503.2204
503.2624
504.2228
505.2206
496.9395
497.6856
499.5325
501.2072
502.5567
506.2184
507.2208
508.2237
510.2081
511.2160
513.2031
m/z

SPECTRUM - simulation :



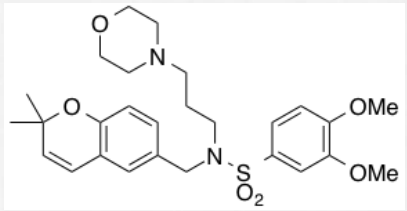
m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
503.2204	503.2210	-1.24	10.5	C26 H35 O6 N2 S

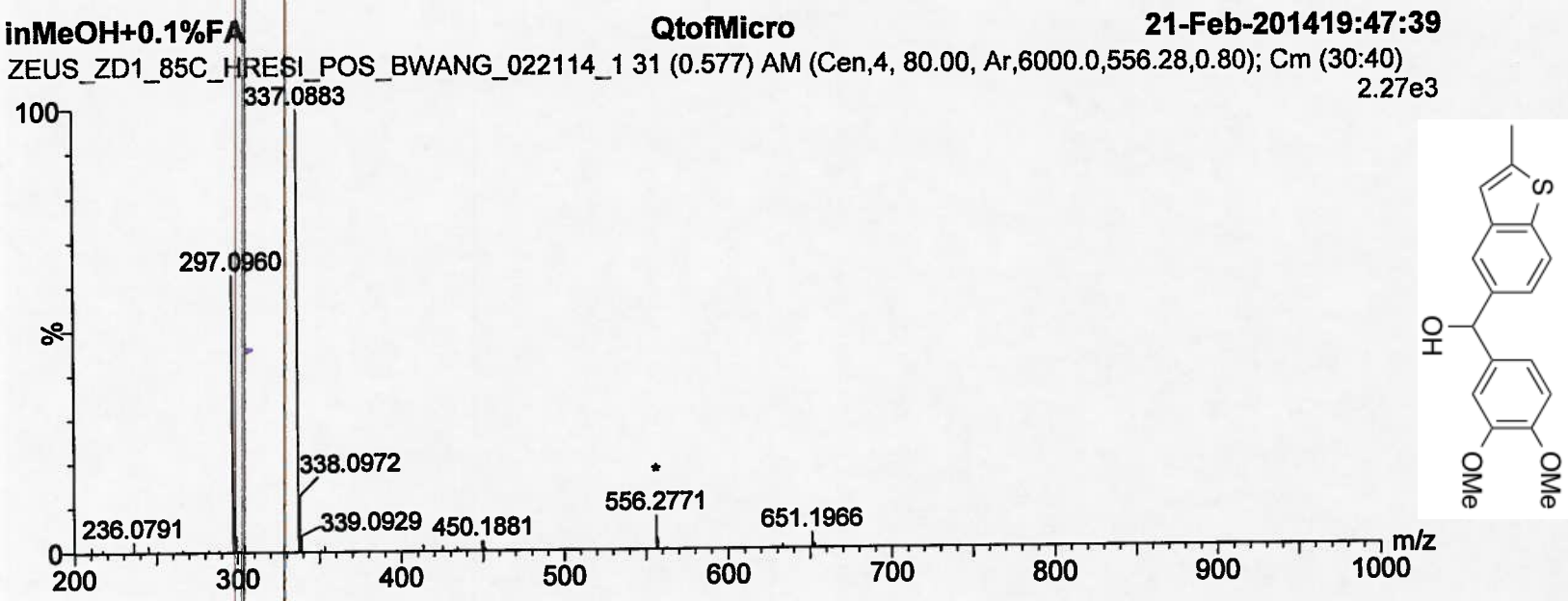




SPECTRUM - simulation :

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
517.2366	517.2367	-0.16	10.5	C27 H37 O6 N2 S





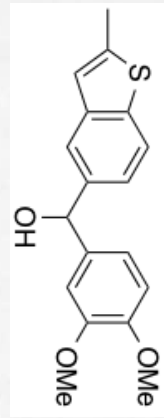
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
138 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 5-80 H: 5-80 O: 1-15 23Na: 0-1 S: 1-2

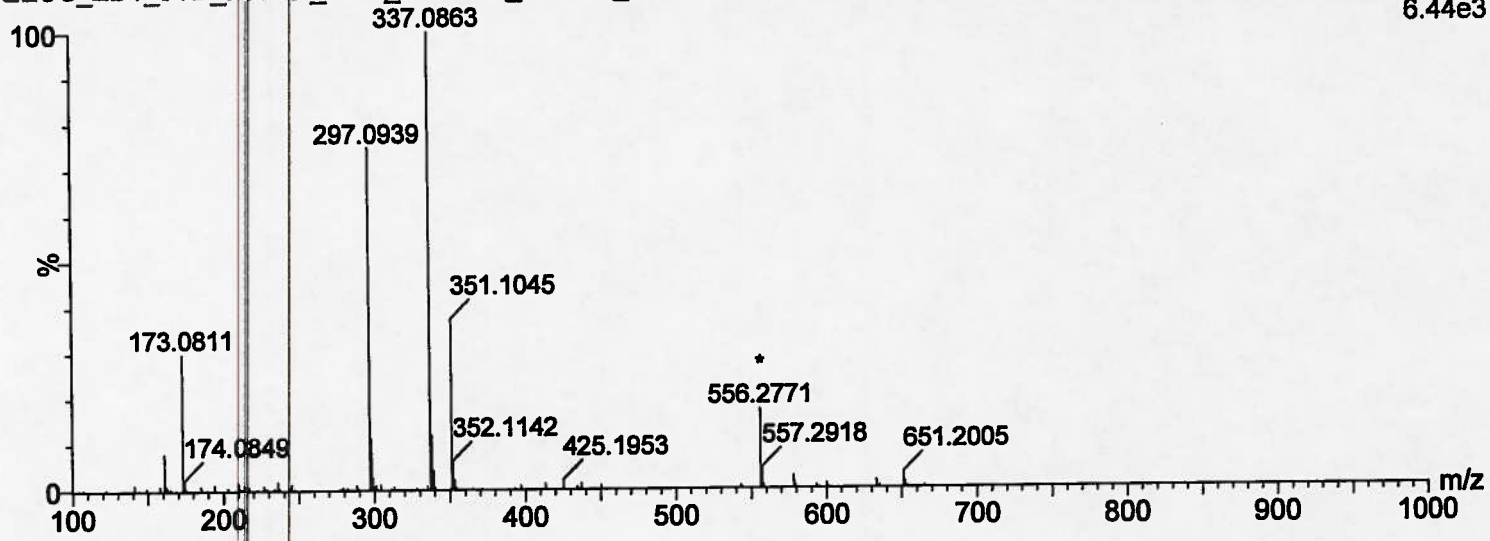
Minimum:				-1.5		
Maximum:		800.0	5.0	200.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula

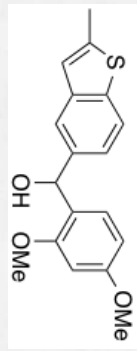
337.0883	337.0874	0.9	2.7	9.5	78.5	C18 H18 O3 23Na S
	337.0898	-1.5	-4.4	12.5	106.0	C20 H17 O3 S



inMeOH+0.1%FA QtofMicro 21-Feb-201420:34:39

ZEUS_ZD1_91D_HRESI_POS_BWANG_022114_1 439 (8.167) AM (Cen,4, 80.00, Ar,6000.0,556.28,0.80); Cm (434:460) 6.44e3





Elemental Composition Report

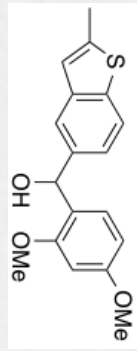
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
226 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 5-80 H: 5-80 O: 1-15 23Na: 0-1 32S: 0-2

Minimum:				-1.5		
Maximum:		800.0	5.0	200.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula

337.0863	337.0865	-0.2	-0.6	17.5	346.9	C23 H13 O3
	337.0874	-1.1	-3.3	9.5	172.6	C18 H18 O3 23Na 32S

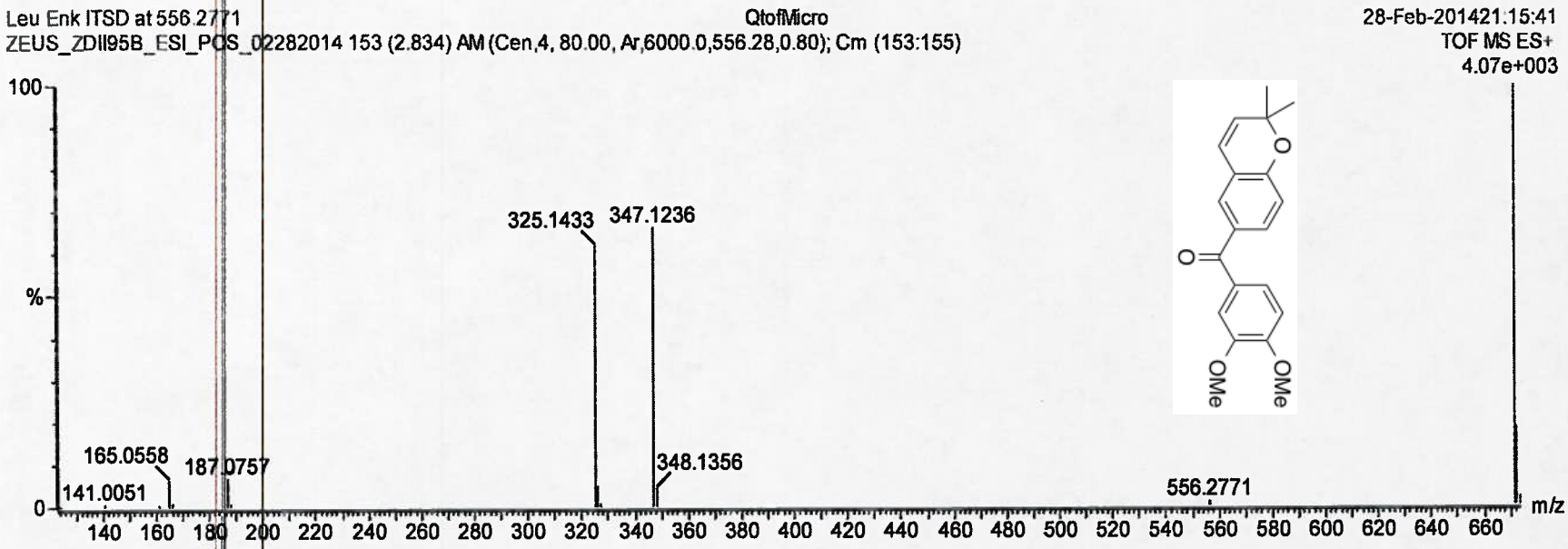
Elemental Composition Report



Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
180 formula(e) evaluated with 3 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 5-80 H: 5-80 O: 1-15 23Na: 0-1 32S: 0-2

Minimum:				-1.5		
Maximum:		800.0	5.0	200.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
297.0939	297.0949	-1.0	-3.4	10.5	48.0	C18 H17 O2 32S
	297.0950	-1.1	-3.7	3.5	12.4	C12 H18 O7 23Na
	297.0925	1.4	4.7	7.5	32.6	C16 H18 O2 23Na 32S

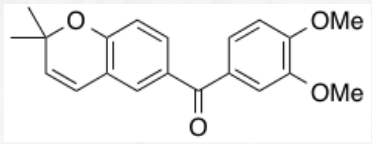


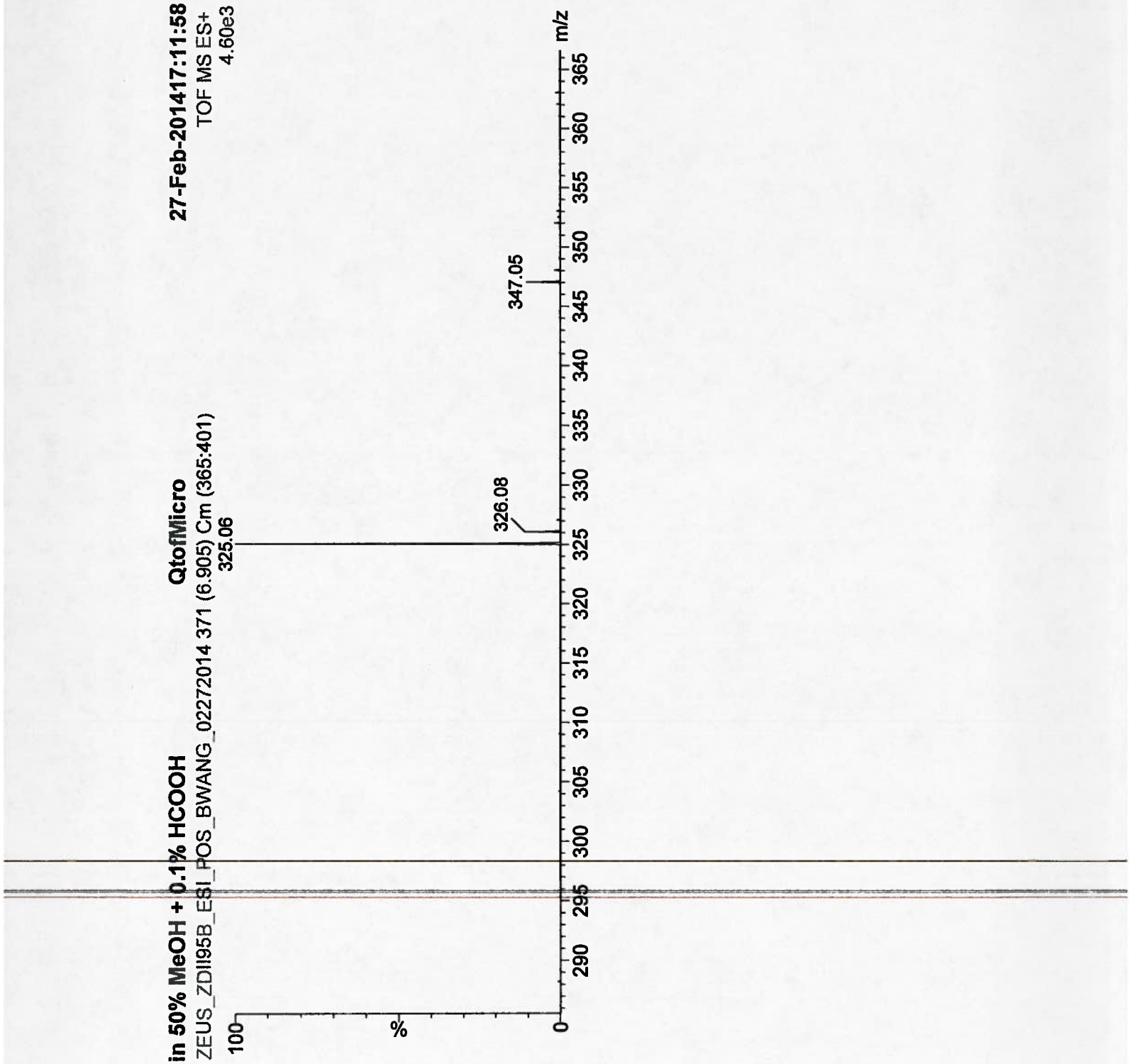
Elemental Composition Report

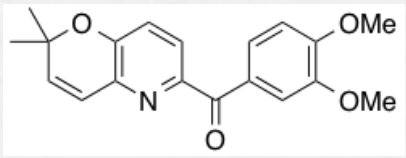
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

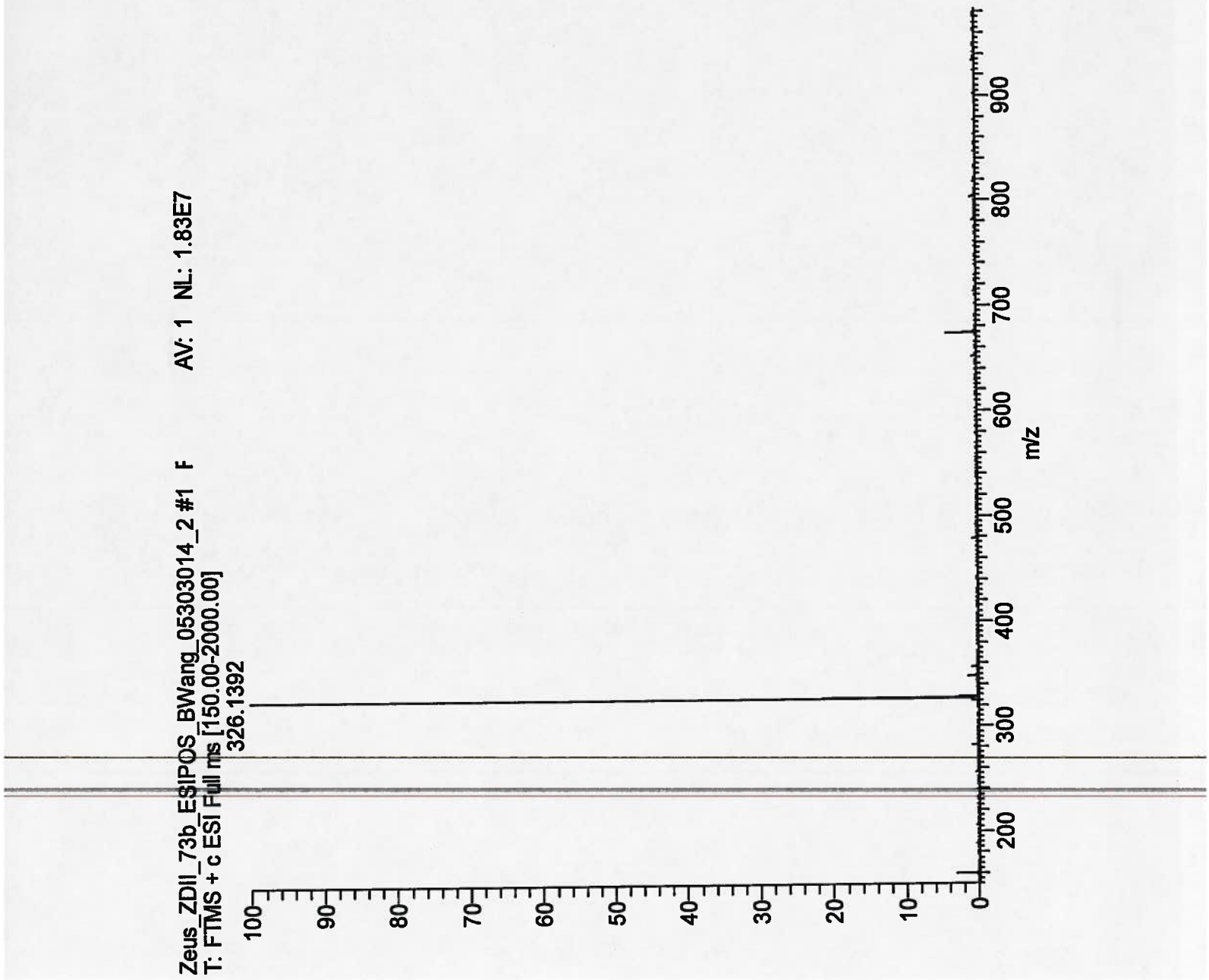
Monoisotopic Mass, Even Electron Ions
56 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 1-80 H: 1-80 O: 1-80

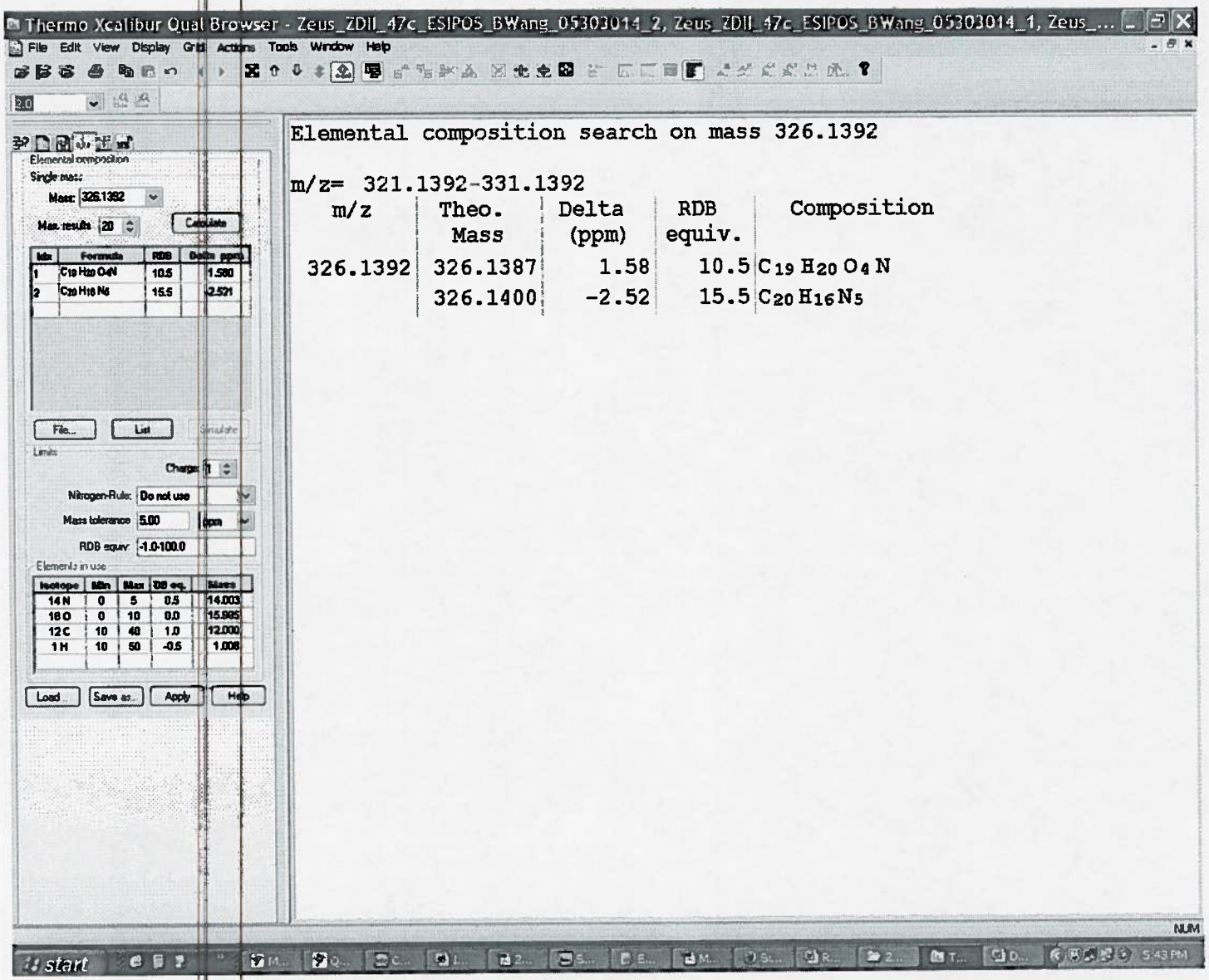
Minimum:				-1.5			
Maximum:		800.0		5.0	200.0		
Mass	Calc. Mass	mDa		PPM	DBE	i-FIT	Formula
325.1433	325.1440	-0.7	-2.2	10.5	362.7		C20 H21 O4

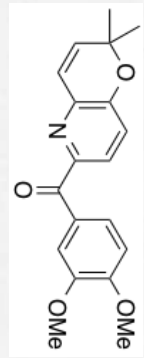

O
OMe
OMe
O

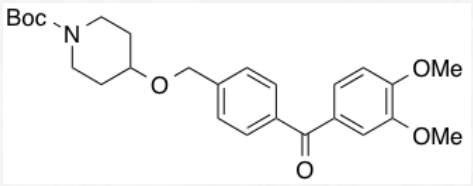

in 50% MeOH + 0.1% HCOOH
ZEUS_ZDII95B_ESI_POS_BWANG_02272014 371 (6.905) Cm (365:401)
QtofMicro
27-Feb-201417:11:58
TOF MS ES+
4.60e3
325.06
326.08
347.05
100
%
0
290
295
300
305
310
315
320
325
330
335
340
345
350
355
360
365
m/z

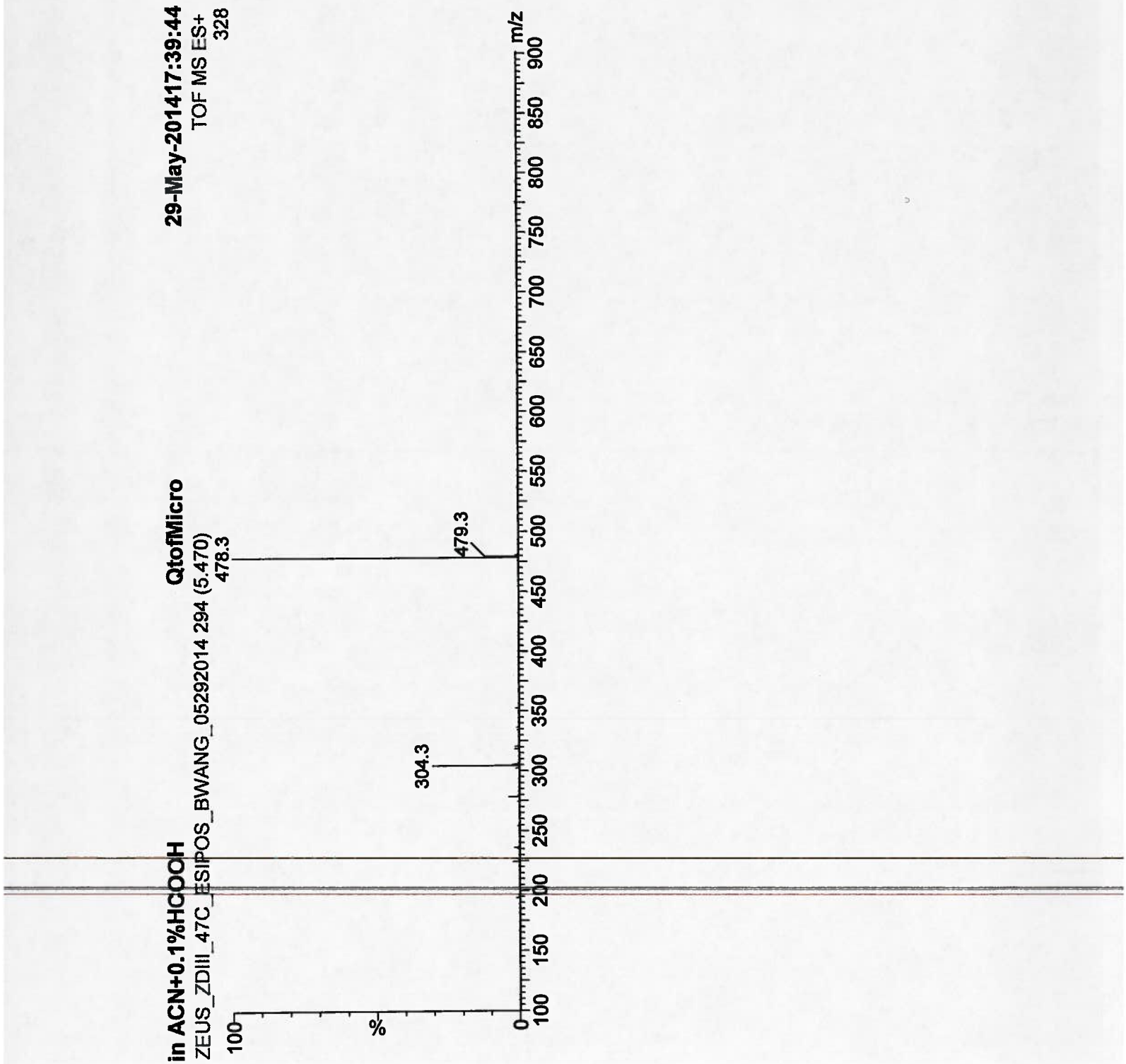

O
N
O
OMe
OMe

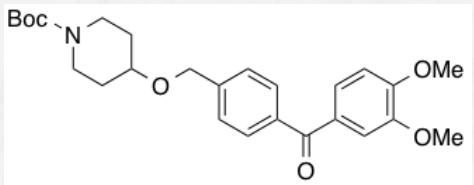

Zeus_ZDII_73b_ESIPOS_BWang_05303014_2 #1 F
T: FTMS + c ESI Full ms [150.00-2000.00]
326.1392
AV: 1 NL: 1.83E7
m/z
0
10
20
30
40
50
60
70
80
90
100
200
300
400
500
600
700
800
900

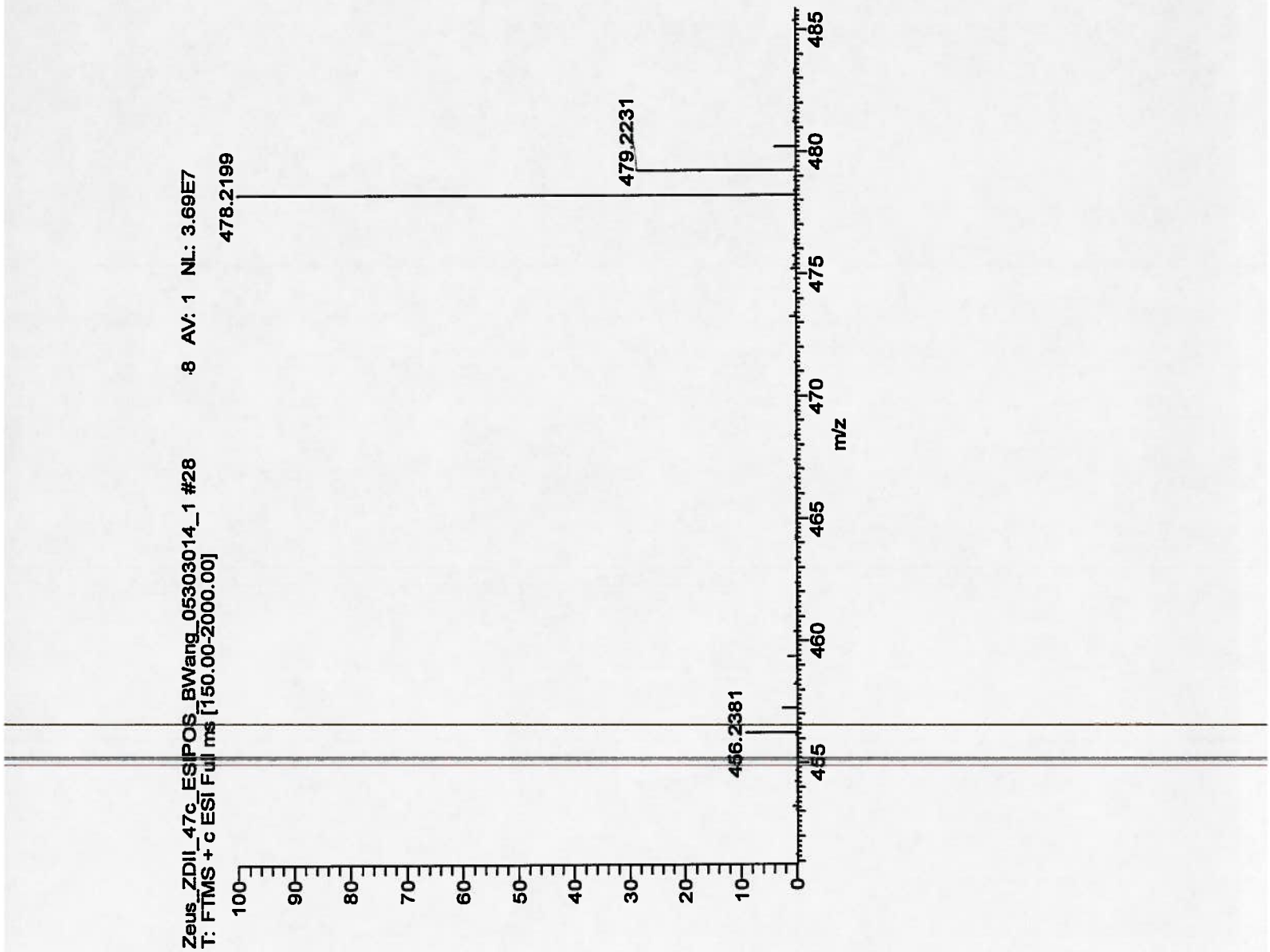

Thermo Xcalibur Qual Browser - Zeus_ZDII_47c_ESIPOS_BWang_05303014_2, Zeus_ZDII_47c_ESIPOS_BWang_05303014_1, Zeus_...
File Edit View Display Grid Actions Tools Window Help
Elemental composition search on mass 326.1392
m/z= 321.1392-331.1392
m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition
326.1392 | 326.1387 | 1.58 | 10.5 | C19 H20 O4 N
326.1400 | -2.52 | 15.5 | C20 H16 N5
Elemental composition
Single mass
Mass: 326.1392
Max. results: 20
Calculate
File...
List
Simulate
Limits
Charge: 1
Nitrogen-Rule: Do not use
Mass tolerance: 5.00 ppm
RDB equiv: -1.0-100.0
Elements in use
Isotope | Min | Max | RDB eq. | Mass
14 N | 0 | 5 | 0.5 | 14.003
16 O | 0 | 10 | 0.0 | 15.995
12 C | 10 | 40 | 1.0 | 12.000
1 H | 10 | 50 | -0.5 | 1.008
Load...
Save as...
Apply
Help
NUM
start
5:43 PM

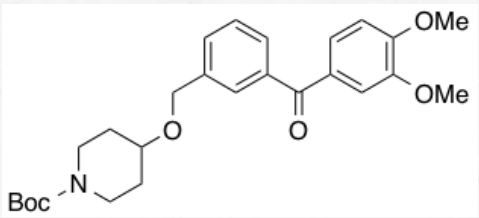

O
N
O
OMe
OMe

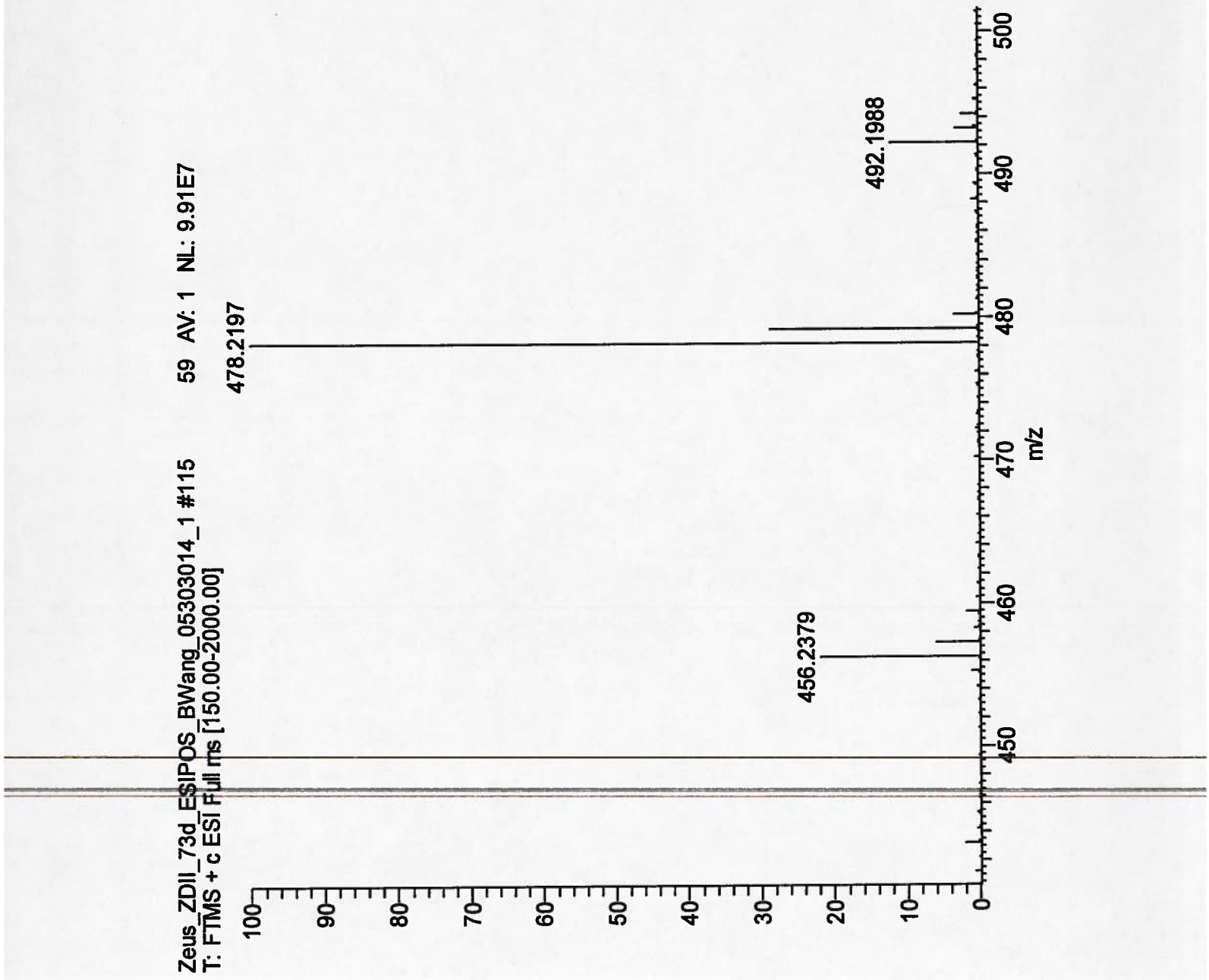

Boc
N
O
OMe
OMe
O

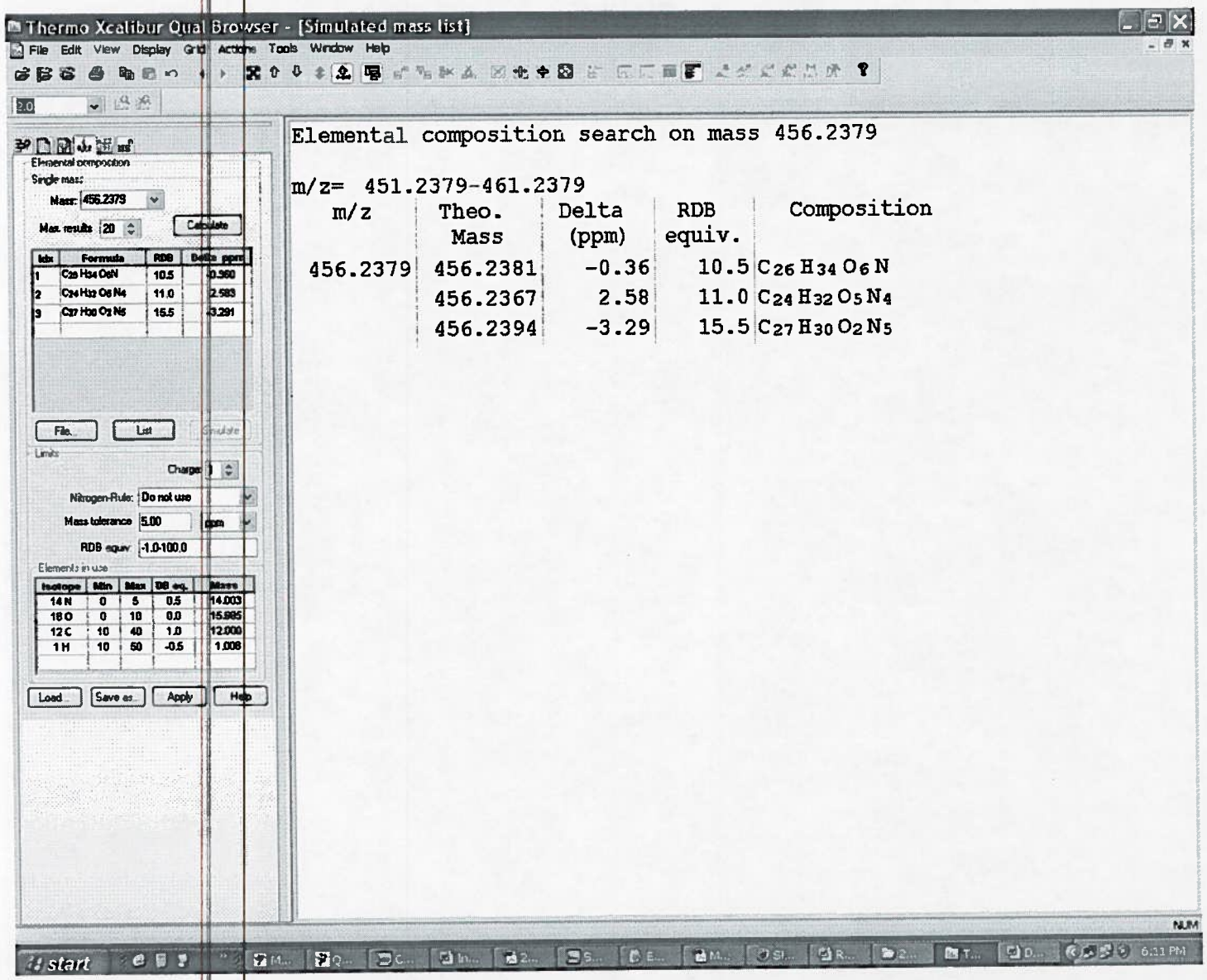

29-May-201417:39:44
TOF MS ES+
328
QtofMicro
in ACN+0.1%HCOOH
ZEUS_ZDIII_47C_ESIPOS_BWANG_05292014 294 (5.470)
478.3
479.3
304.3
100
%
0
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900
m/z

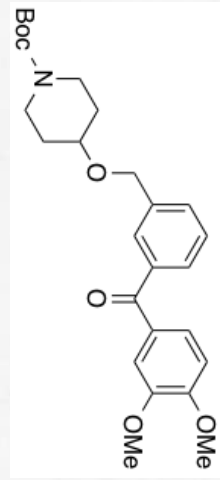

Boc
N
O
OMe
OMe
O

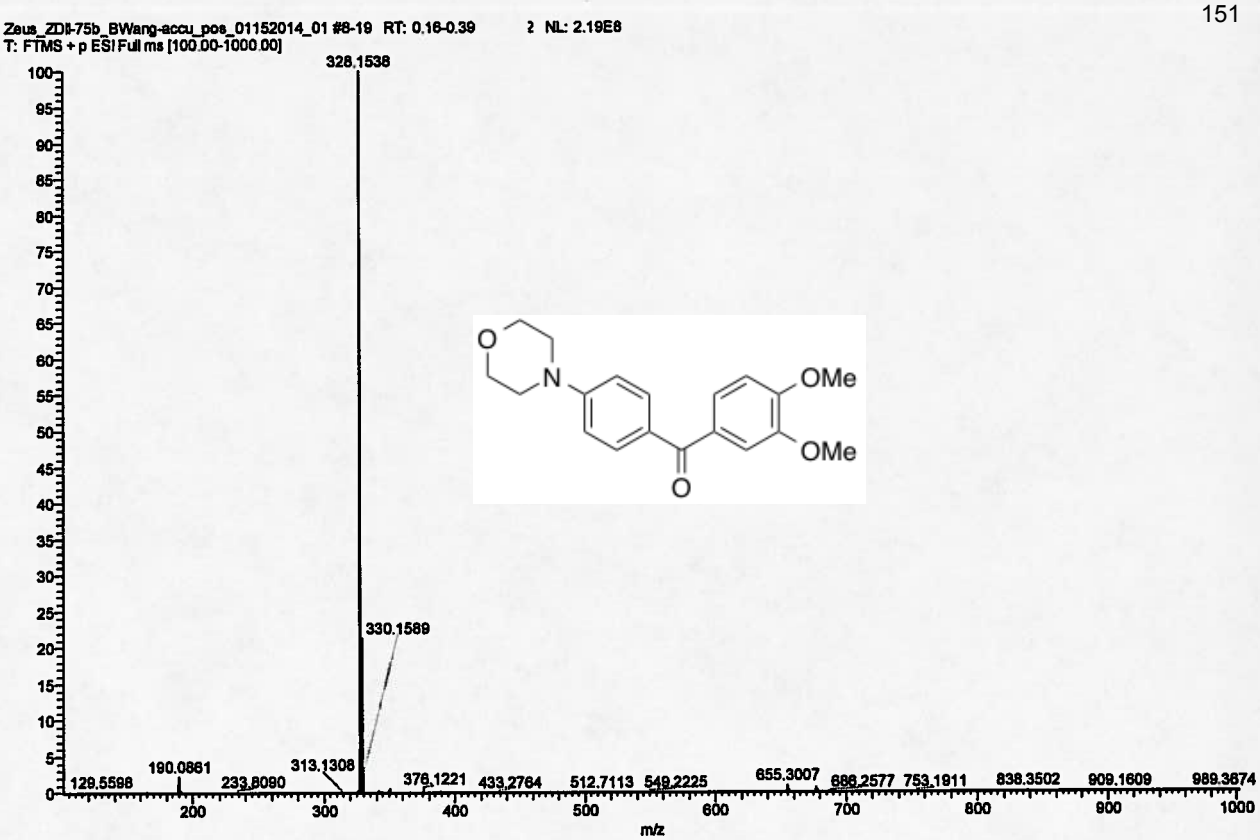

Zeus_ZDII_47c_ESIPOS_BWang_05303014_1 #28
T: FTMS + c ESI Full ms [150.00-2000.00]
8 AV: 1 NL: 3.69E7
478.2199
479.2231
456.2381
m/z

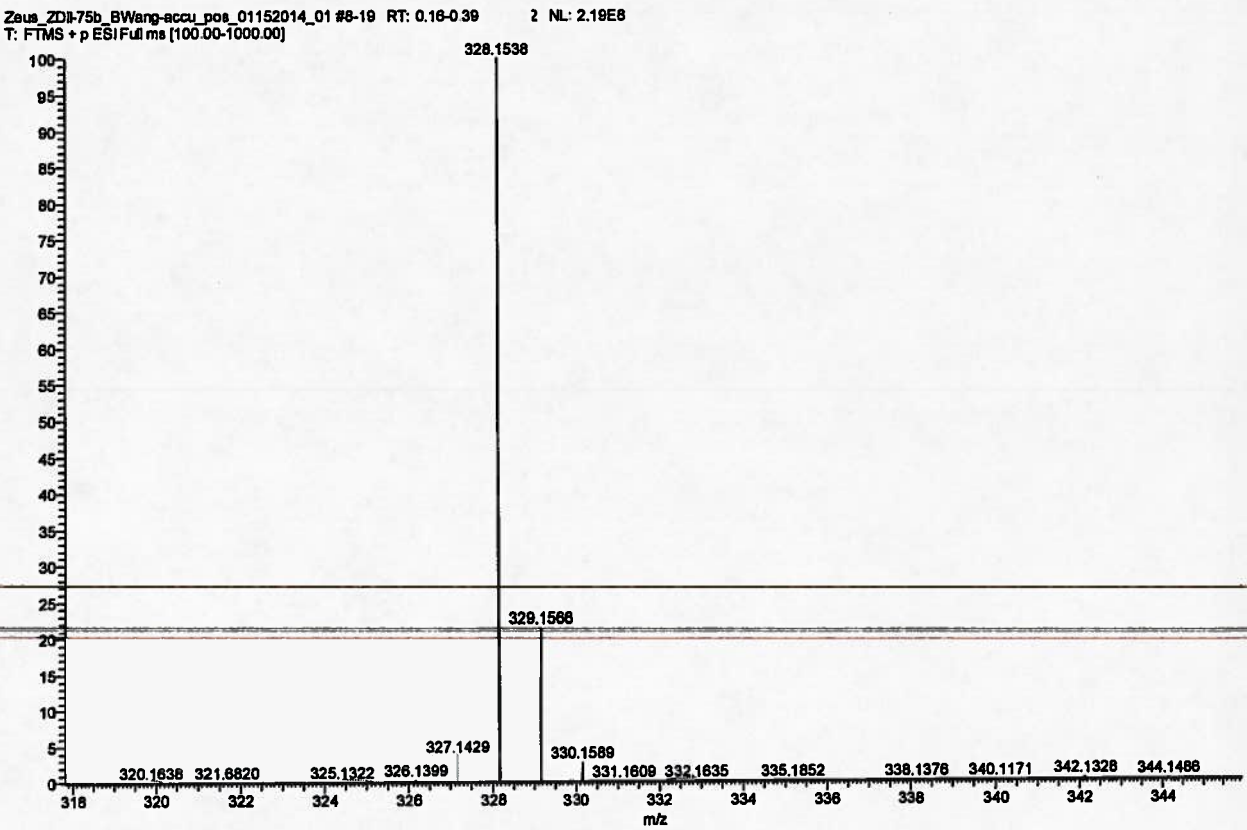

OMe
OMe
O
O
N
Boc


Zeus_ZDII_73d_ESIPOS_BWang_05303014_1 #115
T: FTMS + c ESI Full ms [150.00-2000.00]
59 AV: 1 NL: 9.91E7
478.2197
492.1988
456.2379
m/z
100
90
80
70
60
50
40
30
20
10
0
450
460
470
480
490
500

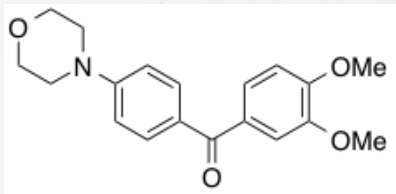

Thermo Xcalibur Qual Browser - [Simulated mass list]
File Edit View Display Grid Actions Tools Window Help
Elemental composition search on mass 456.2379
m/z= 451.2379-461.2379
m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition
456.2379 | 456.2381 | -0.36 | 10.5 | C26 H34 O6 N
456.2367 | 2.58 | 11.0 | C24 H32 O5 N4
456.2394 | -3.29 | 15.5 | C27 H30 O2 N5
start


Boc
N
O
O
OMe
OMe

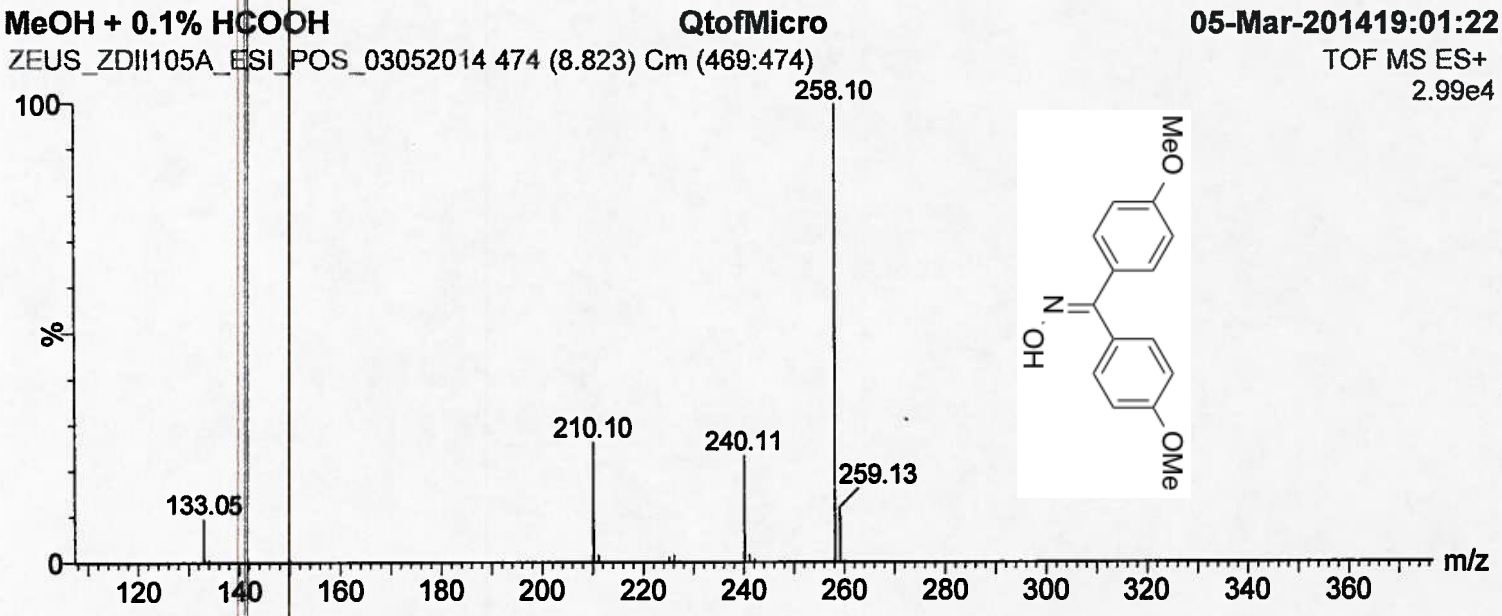

Zeus_ZDll-75b_BWang-accu_pos_01152014_01 #8-19 RT: 0.16-0.39 2 NL: 2.19E8
T: FTMS + p ESI Full ms [100.00-1000.00]
328.1538
330.1589
313.1308
190.0861
129.5598
233.8090
376.1221
433.2764
512.7113
549.2225
655.3007
686.2577
753.1911
838.3502
909.1609
989.3674
O
N
OMe
OMe
O
m/z

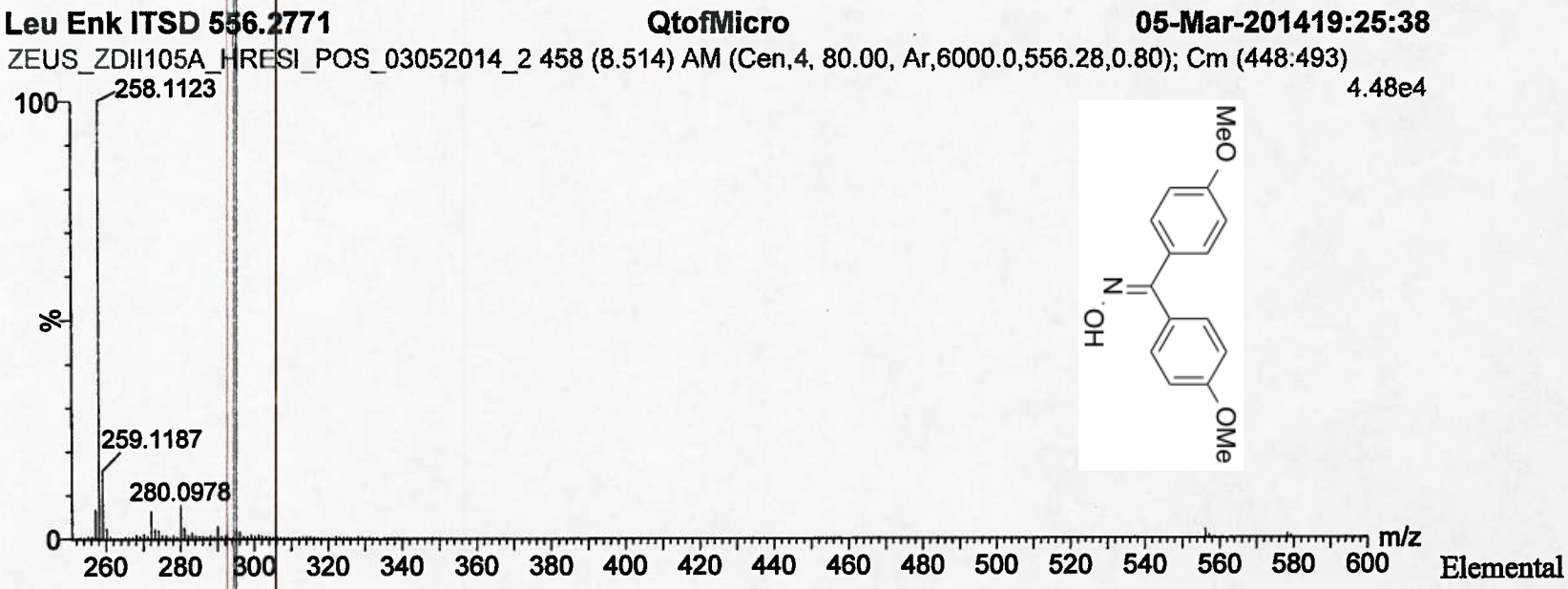

Zeus_ZDll-75b_BWang-accu_pos_01152014_01 #8-19 RT: 0.16-0.39 2 NL: 2.19E8
T: FTMS + p ESI Full ms [100.00-1000.00]
328.1538
329.1566
327.1429
330.1589
320.1638
321.6820
325.1322
326.1399
331.1609
332.1635
335.1852
338.1376
340.1171
342.1328
344.1486
m/z

SPECTRUM - simulation :



m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
328.1538	328.1543	-1.75	9.5	C19 H22 O4 N


MeOH + 0.1% HCOOH
QtofMicro
05-Mar-201419:01:22
ZEUS_ZDII105A_ESI_POS_03052014 474 (8.823) Cm (469:474)
TOF MS ES+
2.99e4
100
%
0
258.10
210.10
240.11
259.13
133.05
120
140
160
180
200
220
240
260
280
300
320
340
360
m/z
MeO
N
OH
OMe

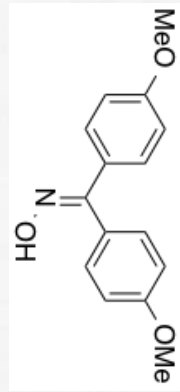

Leu Enk ITSD 556.2771
QtofMicro
05-Mar-201419:25:38
ZEUS_ZDII105A_HRESI_POS_03052014_2 458 (8.514) AM (Cen,4, 80.00, Ar,6000.0,556.28,0.80); Cm (448:493)
4.48e4
258.1123
259.1187
280.0978
100
%
0
m/z
260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600
MeO
N
OH
OMe
Elemental

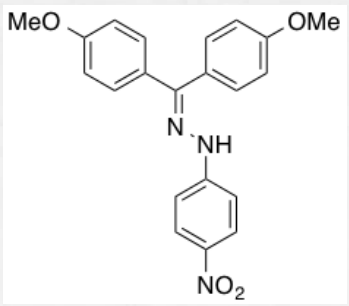
Composition Report

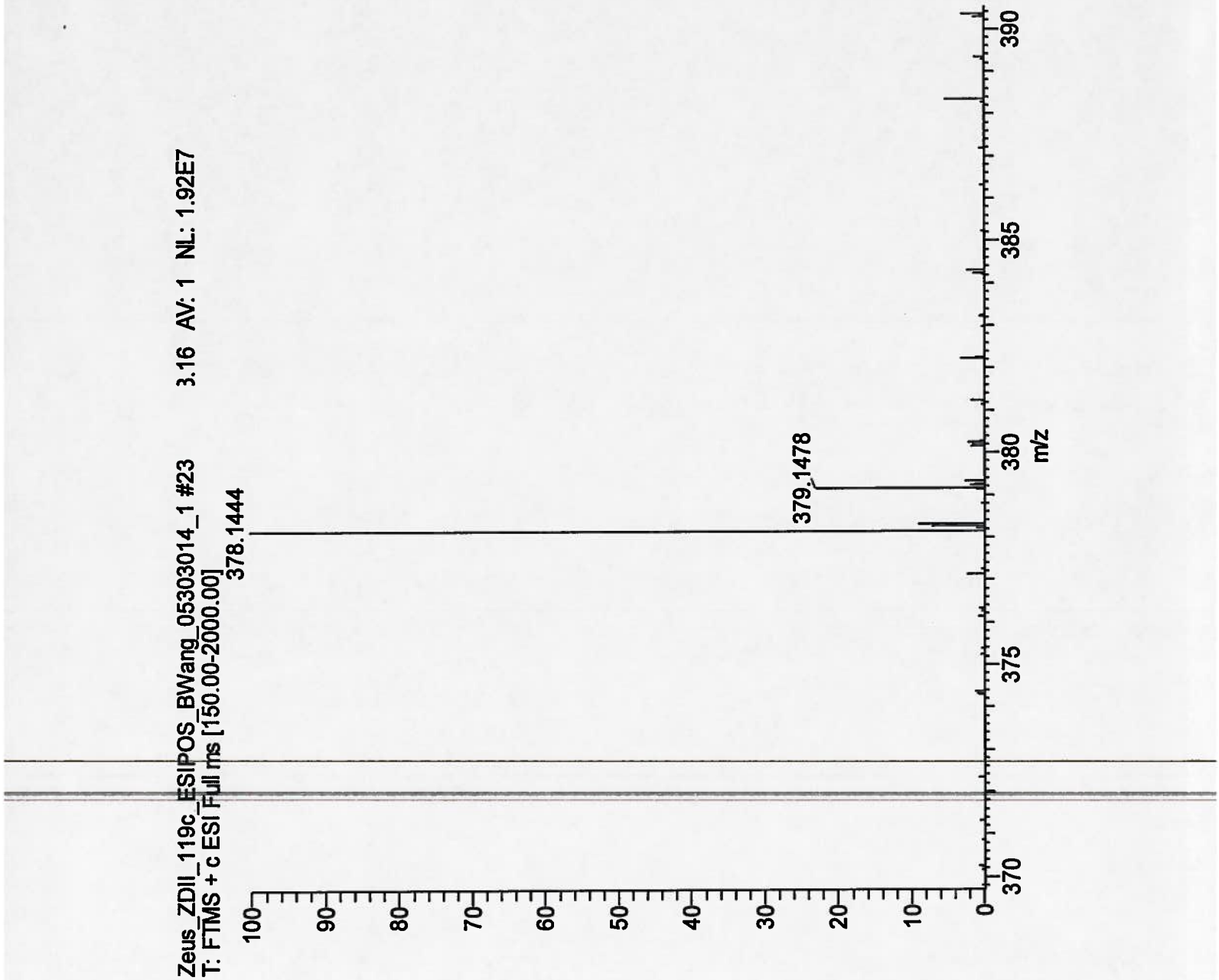
Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 200.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

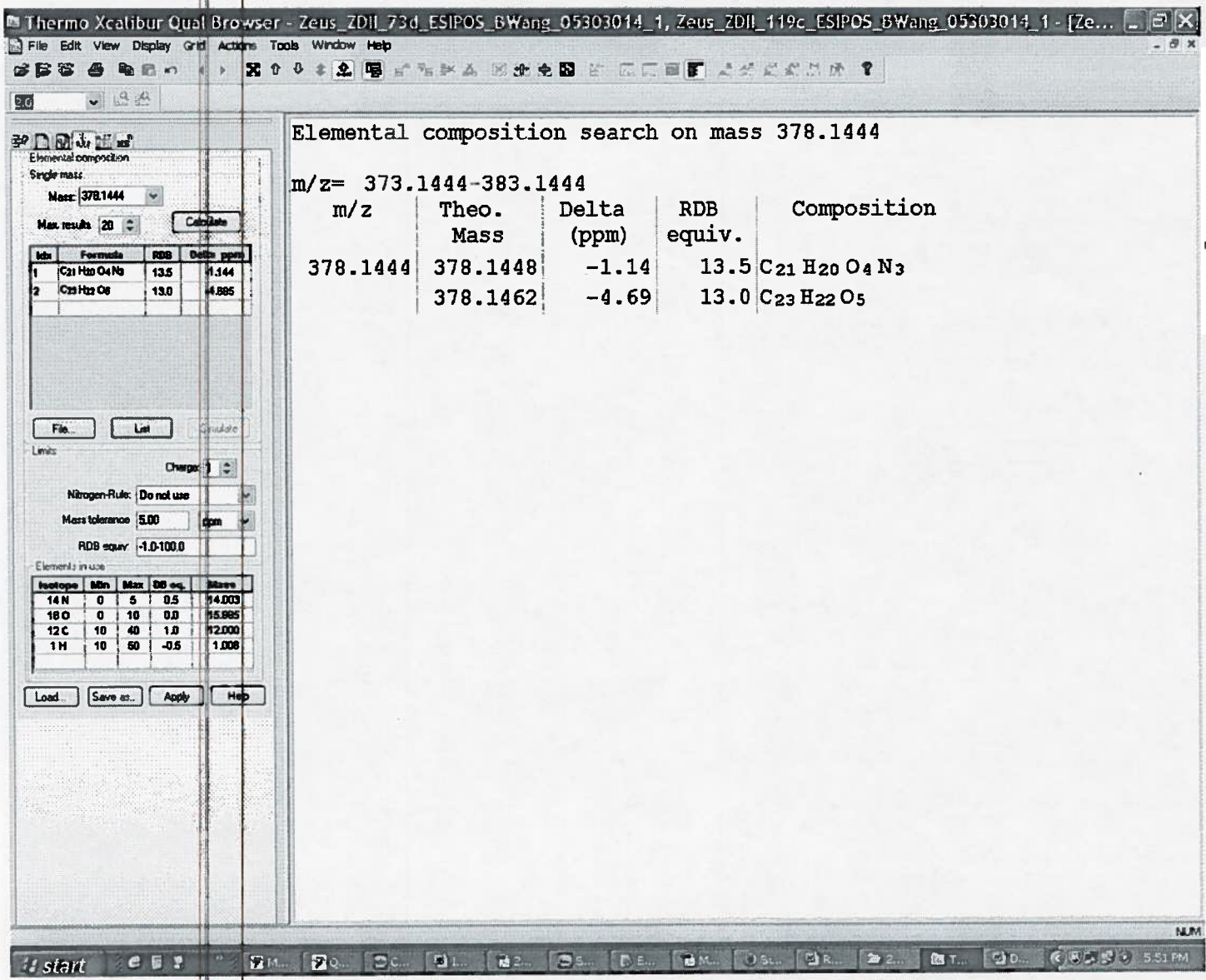
Monoisotopic Mass, Even Electron Ions
267 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 1-80 H: 1-80 N: 1-80 O: 1-80

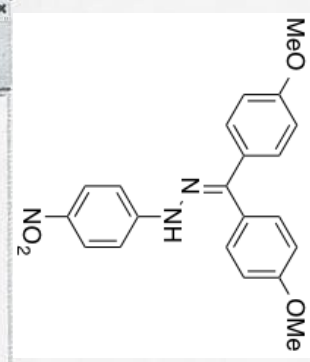
Minimum:			-1.5			
Maximum:		800.0	5.0	200.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
258.1123	258.1130	-0.7	-2.7	8.5	62.4	C15 H16 N O3




MeO
OMe
N
NH
NO2


Zeus_ZDII_119c_ESIPOS_BWang_05303014_1 #23 3.16 AV: 1 NL: 1.92E7
T: FTMS + c ESI Full ms [150.00-2000.00]
378.1444
379.1478
100
90
80
70
60
50
40
30
20
10
0
370
375
380
385
390
m/z


Thermo Xcalibur Qual Browser - Zeus_ZDII_73d_ESIPOS_BWang_05303014_1, Zeus_ZDII_119c_ESIPOS_BWang_05303014_1 - [Ze...
File Edit View Display Grid Actions Tools Window Help
Elemental composition search on mass 378.1444
m/z= 373.1444-383.1444
m/z | Theo. Mass | Delta (ppm) | RDB equiv. | Composition
378.1444 | 378.1448 | -1.14 | 13.5 | C21 H20 O4 N3
| 378.1462 | -4.69 | 13.0 | C23 H22 O5
start
5:51 PM


MeO
OMe
NO2
N
NH